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THE RELATIVE VALUE OF INORGANIC AND ORGANIC IRON IN HEMOGLOBIN FORMATION *

C. A. ELVEHJEM, PH.D.

MADISON, WIS.

The magnitude of the literature that has been published concerning the metabolism of different forms of iron makes it impossible to attempt a complete review of the subject in this short paper. A discussion of much of the early work is also unnecessary in light of the more recently established facts, which lead to an explanation of much of the contradictory evidence presented in the earlier papers on hemoglobin formation. Those who believe that inorganic iron cannot be utilized and that only organic iron is available for hemoglobin formation find little support for their view in the recent work.

Experimental work in both laboratories and clinics has shown that inorganic iron salts when fed under proper conditions can be utilized for the synthesis of hemoglobin. In 1928 Hart, Steenbock, Waddell and Elvehjem [1] demonstrated that inorganic iron, such as ferric chloride, when accompanied by traces of copper can be used as the sole source of iron for the cure of nutritional anemia in rats. This fact has been amply substantiated in a number of different laboratories.[2] Inorganic iron when fed together with proper amounts of copper has been shown to be equally valuable for the cure of nutritional anemia in other animals, such as chickens,[3] pigs [4] and mice.[5]

A few workers,[6] although they admit that copper is the most active supplement to iron, suggest that certain other metals, especially manganese, may also function in promoting hemoglobin formation. Waddell, Steenbock and Hart [7] have shown, however, that manganese is ineffective and have reaffirmed the specificity of copper. Other workers [8] have verified these conclusions.

Drabkin and Waggoner [9] succeeded in curing rats made anemic on a milk diet by feeding a synthetic ration which contained iron but which, they asserted, was exceedingly low in copper, so that they questioned the necessity of copper. Elvehjem and Hart [10] analyzed the synthetic diets used by these workers and found sufficient copper present to account for their activity in hemoglobin regeneration. More recently Drabkin and Miller [11] have suggested that certain amino-acids may supplement iron in the cure of nutritional anemia. Elvehjem, Steenbock and Hart,[12] working with glutamic acid, which Drabkin found to be very effective, have demonstrated that this amino-acid is completely inactive as a supplement to iron when it is properly purified. It is evident, therefore, that inorganic iron can be used directly for hemoglobin formation in animals rendered anemic by milk diets and that copper must be supplied in traces to allow the utilization of this iron. Milk, which has been used so extensively for the production of experimental anemia, is exceedingly low in both iron and copper.

Whipple and Robscheit-Robbins,[13] working with secondary anemia in dogs, produced by continued bleeding, have observed favorable effects when iron salts were administered in the long period anemias. Iron was found to be inert when the anemia period was of short duration. The iron reserves undoubtedly were not depleted in the short period experiments, and this element therefore was not a limiting factor. They [14] found that the daily addition of 40 mg. of iron to the basal ration of each dog produced an average weekly output of 25 Gm. of hemoglobin. Elden, Sperry,

* From the Department of Agricultural Chemistry, University of Wisconsin.

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14. Whipple, G. H., and Robscheit-Robbins, F. S.: Blood Regeneration in Severe Anemia: XVI. Optimum Iron Therapy and Salt Effect, Am. J. Physiol. **92**: 362 (March) 1930.

Robscheit-Robbins and Whipple [15] found that combined copper and iron feeding may at times have an unusually favorable effect and again may not exceed the favorable influence of iron alone. The variable effect of copper in this type of anemia is not surprising since the supply of copper in the dogs is probably not depleted. When the dogs are bled, large amounts of iron are removed; but only traces of copper accompany the blood because it contains a very small amount of this element.[16] The basal ration used also furnished some copper. Generally, then, there was sufficient copper present in the organs of the dogs to stimulate hemoglobin formation, provided the iron was supplied. They conclude that iron salts are much more potent than copper salts for hemoglobin regeneration. This fact is naturally true since iron is the material used in the construction of the hemoglobin molecule, while copper is necessary in only minute amounts as a catalyst. We have a similar relationship in the case of calcium and vitamin D. Vitamin D cannot replace calcium, but it is very essential for the utilization of this element.

Robscheit-Robbins and Whipple [17] report an interesting summation effect when liver or kidney is fed together with iron. Until more is known about the form of iron present in such organs it is difficult to determine whether this effect is due to a more available supply of iron, to an increased supply of copper which stimulates the formation of hemoglobin, or to other factors present in these organs. It is important to remember that in this type of anemia the entire blood is removed and the diet must supply the material necessary for the production of all the blood constituents, while in the anemia produced by a milk diet there is only a deficiency of hemoglobin.

When one turns to the data that have been published on the value of inorganic iron in human anemias, the results are more conflicting, because the causes of the anemia are so variable. In the first place, it is generally accepted today that iron and copper therapy is ineffective in pernicious anemia. Middleton,[18] feeding an iron and copper solution in two cases of pernicious anemia, observed no improvement after fifteen days of treatment. He did note, however, a very sharp rise in the reticulocytes within a few hours after the initiation of the liver extract therapy. Recent work leads me to believe that the material from liver active in pernicious anemia is an organic nitrogenous compound.

Nevertheless, many favorable results have been obtained by the use of inorganic iron in secondary anemias in human beings. The recoveries have been particularly phenomenal in infants, especially those who have been maintained on milk diets for too long periods. Mackay,[19] who has recently summarized her very extensive work with children in London, found a large number of the infants studied to be definitely anemic. This anemia was readily cured in a large percentage of the cases by feeding the infants inorganic iron in the form of iron and ammonium citrate. Copper in sufficient amounts to promote hemoglobin formation was undoubtedly supplied through the iron salts and milk powder used. Dr. Mackay writes: "The presence of active disease may delay or entirely prevent a rise in hemoglobin with iron treatment although the child is suffering from iron deficiency." She says further: "Nevertheless it is wise to give iron, if the digestive tract will tolerate it, in nearly all diseases of infancy accompanied by anemia, even if the cause of the anemia has been a hemorrhage or a streptococcal infection because, whatever the cause, materials for hemoglobin building should be made available for the infant."

Josephs [20] has recently demonstrated the value of iron and copper in the treatment of certain types of anemia in children. Lewis [21] found that iron and copper given in combination to children with nutritional and secondary anemia was more effective than iron given alone. In some cases very little response was noted with iron alone, but rapid recoveries were obtained by the further addition of copper. This result was particularly noticeable in the nutritional series. Mills [22] observed beneficial results when he fed iron and copper to adults suffering from idiopathic anemia.

Keefer and Yang [23] found that liver and iron given in combination to patients with secondary anemia was more effective than either given alone. They also observed that iron alone in the form of ferrous carbonate caused an increase in the rate of hemoglobin regeneration in some forms of secondary anemia. Cabot [24] demonstrated that better results were obtained when liver was fed with ferrous lactate than when iron was fed alone. Powers and Murphy,[25] studying the comparative value of iron, whole liver, and liver extract in the treatment of patients with anemia due to chronic hemorrhage or chronic chlorosis, found that the patients who received iron alone or in combination with whole liver improved most rapidly. They found liver extract to be inert, which is to be expected since it contains very little iron. The recovery was more striking when the liver extract was supplemented with iron than when whole liver was used in conjunction with the extract.

There seems to be little doubt, therefore, that hemoglobin is formed during normal metabolism in mammals from the iron present in the food and that copper, which is also supplied through the food, is necessary for this synthetic process. When the amount of iron or copper in the food becomes insufficient to supply the need either because of a decreased supply of these elements in the food or because of a greater demand for hemoglobin formation, anemia ensues. This insufficiency may be corrected by the addition of inorganic iron and copper, provided the condition is not complicated by infection. The value of liver as the source of iron is not so well established, but the majority of the workers who have studied the relative value of liver and iron have not fed these materials on an equal iron basis.

The question naturally arises, therefore, Is organic iron as valuable for hemoglobin formation as inorganic salts? Also, is copper as necessary when organic iron

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25. Powers, J. H., and Murphy, W. P.: The Treatment of Secondary Anemia, J. A. M. A. **96**: 504 (Feb. 14) 1931.

is fed as when the inorganic form is used? In fact, several workers have suggested to me that copper is necessary only when inorganic salts are used as the source of iron. In other words, they still hold part of Bunge's [26] old theory that iron occurs in food as complicated organic compounds which are absorbed and assimilated as such and built directly into hemoglobin. When organic iron is fed, it is used directly; but when

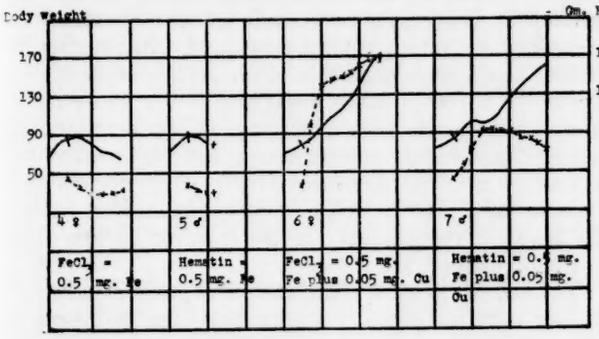

Chart 1.—Results obtained when ferric chloride and hematin with and without copper were added to the basal diet of whole cow's milk. The additions were made seven days per week. The solid line represents body weight, and the broken line represents hemoglobin in grams per hundred cubic centimeters of blood.

inorganic iron is supplied, copper must be added to allow its utilization. The following experiments were initiated to answer these questions.

Before proceeding to the experimental work it is well to consider what is meant by organic iron. Food iron and organic iron is used interchangeably in the literature. This is obviously incorrect because the plant and animal materials which make up food contain both the inorganic and organic forms of iron. Very little work has been done on the iron compounds present in plant and animal tissues, but from the data that have been presented one is probably safe in assuming that the largest part of the organic iron is in the form of hematin compounds. Keilin [27] has shown that cytochrome, which is widely distributed in all cells of aerobic organisms, is composed of hematin compounds. He [28] has also demonstrated that all aerobic organisms contain a free unbound hematin similar to the protohematin of hemoglobin. This compound can easily be observed spectroscopically in cells such as the endosperm of cereals, especially in oatmeal flour or wheat flour. Anson and Mirsky [29] suggest that about one third of the iron of bakers' yeast and the wing muscles of bees is in the form of hematin. Hill,[30] using a new reagent which reacts only with inorganic iron in the presence of hematin, found that the entire iron content of egg yolk consists of inorganic iron. This view is directly opposed to that of Bunge,[26] who stated that all the iron was present in hematogen, which held iron in such firm organic combination that it gave none of the ordinary reactions of iron salts.

I [31] have found, by the use of Hill's method, that at least one half of the total iron in yeast is present in the inorganic form. The iron compounds in food require a great deal more attention, but the data already available strongly indicate that a large part of the organic iron occurs in the form of hematin. Hematin was therefore used as a source of organic iron in the feeding trials presented in this paper.

26. Bunge, G.: Textbook of Physiological and Pathological Chemistry, Philadelphia, P. Blakiston's Son & Co., 1902, chapter 25.
27. Keilin, D.: Cytochrome and Respiratory Enzymes, Proc. Roy. Soc. London, series B **104**: 206 (Feb. 4) 1928.
28. Keilin, D.: A Comparative Study of Turacin and Hematin and Its Bearing on Cytochrome, Proc. Roy. Soc. London, series B **100**: 129, 1926.
29. Anson, M. L., and Mirsky, A. E.: Heme and Tissue Iron, J. Gen. Physiol. **12**: 401 (Jan. 20) 1929.
30. Hill, R.: Methods for the Estimation of Iron in Biological Material, Proc. Roy, Soc. London, series B **107**: 205 (Nov.) 1930.
31. Elvehjem, C. A.: The Rôle of Iron and Copper in the Growth and Metabolism of Yeast, J. Biol. Chem. **90**: 111 (Jan.) 1931.

EXPERIMENTAL

Albino rats were used as the experimental animals in this work because they have been used so extensively in the studies on iron metabolism. The rats were made anemic according to the method outlined by Elvehjem and Kemmerer.[32] When the animals were distinctly anemic (below 4 Gm. of hemoglobin per hundred cubic centimeters of blood) they were placed in individual cages with screen bottoms. The milk diet was continued and the various materials to be tested were added. The hemoglobin values were determined weekly by the Newcomer method with a standardized Bausch and Lomb filter and reported as grams per hundred cubic centimeters of blood.

Ferric chloride was used as a source of inorganic iron. It was prepared from iron wire and purified to remove traces of copper. The ferric chloride was dissolved in water and a sufficient amount of this solution was added to the milk daily to supply 0.5 mg. of iron. Hemin was used as the source of organic iron. The preparation of the hemin is described in an earlier paper.[33] Extreme care was taken during its preparation to prevent copper contamination; 0.333 Gm. of hemin was dissolved in a small amount of dilute ammonium hydroxide and diluted to 25 cc. with redistilled water. One cubic centimeter of this solution was equivalent to 13.3 mg. of hemin or 1 mg. of iron; 0.5 cc., equivalent to 0.5 mg. of iron, was fed daily to the rats. The copper was supplied as copper sulphate.

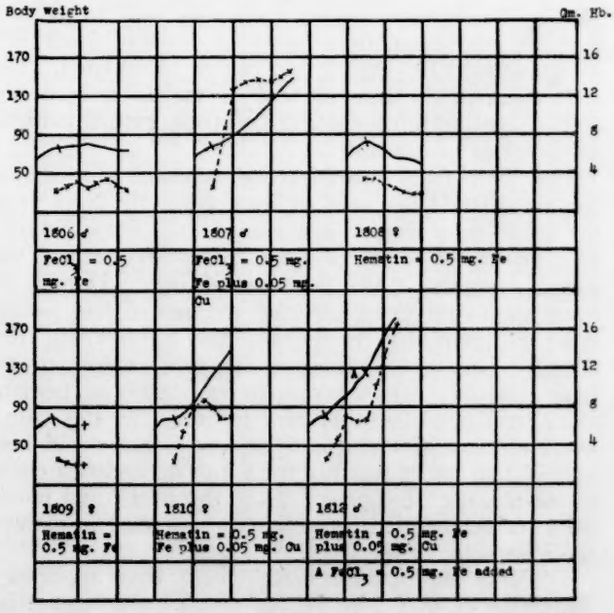

Chart 2.—Further results showing effect of ferric chloride and hematin, when fed with and without copper, on hemoglobin regeneration in anemic rats.

The hemoglobin and weight records of rats from two litters are given in the accompanying charts. These are typical results. Of the rats recorded in chart 1, one was given ferric chloride, one hematin, one ferric

32. Elvehjem, C. A., and Kemmerer, A. R.: An Improved Technic for the Production of Nutritional Anemia in Rats, J. Biol. Chem. **93**: 189 (Sept.) 1931.
33. Elvehjem, C. A.: The Preparation of Standard Acid Hematin Solutions from Hemin, J. Biol. Chem. **93**: 203 (Sept.) 1931.

chloride plus copper, and one hematin plus copper. In chart 2, one of the rats received ferric chloride, one ferric chloride plus copper, two hematin, and two hematin plus copper. Rat 1812 was given ferric chloride in addition to hematin after no further improvement was noted on the hematin diet.

The results obtained with the rats fed ferric chloride, and ferric chloride plus copper, merely reaffirm all the earlier conclusions that inorganic iron alone is inactive but that the same iron in the presence of copper is readily utilized for hemoglobin formation. The rats receiving an equivalent amount of iron in the form of hematin showed no improvement when the hematin was fed alone. This demonstrates that animals can utilize organic iron, in the absence of copper, to no greater advantage for hemoglobin formation than inorganic iron. The most striking results are those obtained with rats receiving both hematin and copper. The hemoglobin values show some improvement but the recovery is neither so rapid nor so complete as when ferric chloride is the source of iron. In no case did the hemoglobin reach figures above 9 Gm. per hundred cubic centimeters. When the rats grew faster, even this figure was not maintained and the values dropped to from 6 to 7 Gm. When ferric chloride was fed with copper, values of from 13 to 14 Gm. were reached in two weeks and these values were maintained indefinitely. In the case of rat 1812 the hemoglobin remained at 6 to 7 Gm. per hundred cubic centimeters as long as hematin was supplying the iron; but as soon as ferric chloride was supplied in addition to the hematin, the hemoglobin increased to 17 Gm. in three weeks' time.

The maximal stimulus for hemoglobin formation was present, but the animal was unable to obtain sufficient iron from the hematin to allow construction of hemoglobin. These results point rather strongly to the fact that all iron compounds must be broken down into inorganic salts before the iron can be assimilated. The differences in the iron content of the livers from the animals getting ferric chloride and those getting hematin support this conclusion.

The liver from rat 7 getting hematin plus copper contained 0.024 per cent of iron, while the liver from rat 1812, on a similar diet except that ferric chloride was also given for three weeks before the animal was killed, contained 0.117 per cent of iron. During the three weeks on ferric chloride the animal had assimilated sufficient iron to increase the hemoglobin from 7 to 17 Gm. and to increase the iron content of the liver fivefold. The liver from rat 1808, on hematin alone, contained 0.08 per cent of iron. In this case a small amount of the iron from the hematin had been assimilated, but it was not built into hemoglobin owing to the absence of copper. Since the iron could not be used for hemoglobin formation, it was used to increase the iron store in the liver.

Whipple and Robscheit-Robbins [34] have reported a utilization of only 5 to 20 per cent of the hemoglobin in red blood cells when they were fed to dogs. Lintzel [35] likewise found that hemoglobin was not as effective in blood regeneration as iron salts. Undoubtedly both the hemoglobin used in these experiments and the hematin used in my experiments were changed to hemin by the hydrochloric acid in the stomach and, therefore, the availability of the same compound was investigated.

34. Whipple, G. H., and Robscheit-Robbins, F. S.: Assimilation and Conservation of Bile Pigment, Blood Hemoglobin and Muscle Hemoglobin, Am. J. Physiol. **83**: 60 (Dec.) 1927.

35. Lintzel, Wolfgang: Zur Frage des Eisenstoffwechsels: II. Mitteilung Eisen und Blutfarbstoffbildung, Ztschr. f. Biol. **87**: 97 (Feb. 1) 1928.

The results presented in this paper show that the limitations of liver in the cure of secondary anemias, which have been observed by different workers, is due to a lack of available iron. Liver itself does not supply large amounts of iron. One hundred grams of fresh beef liver contains only 8 mg. of total iron,[36] and of this total a considerable amount is organic iron which is utilized to only a small extent. It is evident that further studies on the amount and quality of the iron present in food materials used for the treatment of secondary anemias are very necessary. In practice the limitation of such organs as liver as a source of iron should be borne in mind, especially if the cause of the anemia is a specific iron deficiency. Certain commercial preparations, highly recommended for the treatment of secondary anemia because of their large organic iron content, may also be deficient in available iron because the hematin compounds are not readily broken down in the digestive tract.

The relatively small amount of inorganic iron in most of our food materials is a fortunate condition because, if inorganic iron, which is catalytically active in many oxidation processes, were present in large quantities, many of the valuable organic factors found in foods would be destroyed. Under ordinary conditions the animal organism can obtain sufficient iron from the directly available inorganic and the partially available organic iron in its food to supply the needs. It is only in those cases in which the normal iron supply has been interrupted that one must turn to an increased supply greater than that furnished by an average well balanced diet. When such additional iron is required, one must rely on iron compounds which are more available than hematin.

SUMMARY

1. In the absence of copper, organic iron (hematin) is as ineffective as inorganic iron (ferric chloride) for the cure of nutritional anemia in rats.

2. In the presence of copper, organic iron promotes a partial cure of the anemia in rats, but the regeneration is neither so rapid nor so complete as the recovery obtained when ferric chloride is used as the source of iron.

3. The hemoglobin content of the blood of rats, which remained at from 6 to 7 Gm. per hundred cubic centimeters as long as hematin and copper was supplied, increased to 16 Gm. per hundred cubic centimeters in three weeks when ferric chloride was added to the diet.

4. The iron content of the livers from the different animals demonstrates that the decreased activity of the organic iron is due to the inability of the rat to assimilate the iron present in the hematin molecule.

36. Elvehjem, C. A., and Peterson, W. H.: The Iron Content of Animal Tissues, J. Biol. Chem. **74**: 433 (Sept.) 1927.

The Methods of Science.—To observe the phenomena of life, to cultivate observation, to call to aid experimentation, to know the true from the false—these are surely the methods of science, and inasmuch as the doctor uses them, he employs science even in his daily routine work. When he adds to this a perfection in detail, a sense of proportion, and the ability to regard the problem as a whole, placing emphasis on those features that are of true importance, suppressing those matters that are secondary or that form but a background to the problem, he then becomes a true artist. It is not likely that he will become in either instance a creative scientist or a creative artist; for the creative imagination is rare indeed, but lacking this, he still works as a scientist with the sensitiveness of an artist.—Longcope, W. T.: Methods and Medicine, *Bull. Johns Hopkins Hosp.* **50**:4 (Jan.) 1932.

THE PARENTERAL USE OF LIVER EXTRACT IN PERNICIOUS ANEMIA *

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This report deals with the effects of a simple liver extract for parenteral use in the treatment of pernicious anemia. Although many patients with this disease have no great difficulty in consuming sufficient liver to maintain an essentially normal state of health, the introduction of an extract of liver and of stomach substance as a substitute for liver has made the task easier for some of them. There are circumstances, however, in which it may be of distinct importance to have available an actively potent substance which may be given parenterally.

A number of papers have appeared recently recording the results of parenteral treatment with various liver extracts in small series of cases. Gänsslen [1] in 1930 reported on the successful use of daily intramuscular injections of an extract prepared from 5 Gm. of liver. Similar good results have been reported by Schottmüller,[2] van Leeuwen,[3] Selander [4] and others. Castle and Taylor [5] obtained gratifying results following the intravenous use of a liver extract but reported rather severe reactions in about a third of the cases treated. None of the reactions were serious. Strauss, Taylor and Castle [6] later described a method for preparing a liver extract which was used successfully in the treatment of four patients by the daily intramuscular injection of 2 cc. (prepared from 10 Gm. of liver). Wilkinson [7] also reported the use of a "highly purified" liver preparation used both intravenously and intramuscularly with "striking results" in six patients. It is not difficult to visualize the value of a substance for parenteral use which may be given easily and safely and which is inexpensive and readily available for use.

PREPARATION AND METHOD OF USE OF EXTRACT

The first extract used intramuscularly in the cases reported in this paper was prepared in the laboratory of the Peter Bent Brigham Hospital [8] as a simple aqueous solution of liver fraction G (Cohn).[9] Sterilization of the aqueous extract was effected by boiling for four or five minutes. Subsequent extracts used for intramuscular injection and those which have been used intravenously were prepared with the collaboration of Dr. Guy W. Clark of the Lederle Laboratories.[10] This extract is an aqueous solution of fraction G (Cohn) which has been passed through vegetable charcoal, the reaction adjusted to approximately p_H 6.8, the volume altered so that 5 cc. contains the material obtained from 100 Gm. of liver and the finished product passed through a Berkefeld filter. The addition of 0.5 per cent phenol as a preservative to certain lots of extract has not altered its potency.

More recently an extract has been prepared in an essentially similar manner but of greater potency, so that the material obtained from 100 Gm. of liver is contained in 3 cc. of extract.

Thirty patients have been treated by means of the liver extract, and the results are recorded in this paper. Of this number twenty-five received intramuscular injections, usually in the gluteal muscles. These were not given daily but usually at intervals, depending on the circumstances under which treatment was carried out. Hospitalized patients in relapse with red blood cell and hemoglobin level considerably subnormal were usually given from two to four successive injections of 5 cc. of extract prepared from 100 Gm. of liver. After a lapse of from ten days to three weeks, further treatment was given as desired. Ambulatory patients were given generally single intramuscular injections at intervals of from four to seven or more days. For reasons to be discussed later in this paper, a few patients were given daily injections of smaller amounts of extract.

Since the injections of the first type of extract were followed by pain of varying degree, usually at from two to four minutes after the injection, from 1 to 2 cc. of a 2 per cent solution of procaine hydrochloride was introduced through the needle in situ. As there has been little or no pain resulting from the injection of the last extract described, it has been unnecessary to use procaine preceding these.

A small group of patients have received treatment during a relapse in the disease principally by intravenous injection of the same extract and in amounts essentially similar to those used intramuscularly. These injections have been given slowly at the rate of approximately 1 cc. per minute with care to observe any signs of immediate reaction and in some instances of change in blood pressure.

During the period of expected increase, reticulocyte counts were made, usually daily (in some patients more frequently), from smears of the blood made on cover slips previously prepared with a dry film of 0.5 per cent alcoholic solution of brilliant cresyl blue.[11] Only those cells containing definite lines or masses of reticulum have been counted as reticulocytes. Red blood cell counts taken at frequent intervals indicated the course of further improvement and the need for subsequent treatment.

INTRAVENOUS TREATMENT

The liver extract has been used intravenously as the principal form of parenteral administration in four patients. A somewhat detailed description of the patients who received the extract in this manner will serve as an example of the results obtained and in the first patient as a comparison between the results obtained by this method and those observed following the ingestion of liver.

The first patient is a man, aged 54, who entered the hospital in June, 1930, for the first time, complaining of weakness over a period of two months. A diagnosis of pernicious anemia was made, and on June 14 he was started on 300 Gm. of raw liver pulp by mouth daily. An early satisfactory response occurred and continued until his discharge, July 19. He was seen in the blood clinic of the outpatient department, July 29, and again,

* From the Medical Clinic of the Peter Bent Brigham Hospital.

1. Gänsslen, M.: Ein hochwirksamer injizierbarer Leberextract, Klin. Wchnschr. **9**: 2099 (Nov. 8) 1930.
2. Schottmüller, H.: Further Experiences with Liver Therapy in Pernicious Anemia, München. med. Wchnschr. **78**: 432 (March 13) 1931.
3. van Leeuwen, H. C.: Treatment of Pernicious Anemia by Intravenous Administration of Liver Extract, Nederl. tijdscher. v. geneesk. **75**: 4425 (Aug.) 1931.
4. Selander, A.: Liver Extract Suitable for Injection, Hygiea (Stockholm) **93**: 625 (Aug.) 1931.
5. Castle, W. B., and Taylor, F. H. L.: Intravenous Use of Extract of Liver, J. A. M. A. **96**: 1198 (April 11) 1931.
6. Strauss, M. B.; Taylor, F. H. L., and Castle, W. B.: Intramuscular Use of Liver Extract, J. A. M. A. **97**: 313 (Aug. 1) 1931.
7. Wilkinson, J. F.: Injections of Highly Purified Liver Preparations in Pernicious Anemia, Lancet **2**: 791 (Oct. 10) 1931.
8. This simple extract as first used intramuscularly was suggested by Dr. Henry A. Christian.
9. Cohn, E. K.; Minot, G. R.; Fulton, J. R.; Ulrichs, H. F.; Sargent, F. C.; Weare, J. H., and Murphy, W. P.: The Nature of the Material in Liver Effective in Pernicious Anemia, J. Biol. Chem. **74**: 69 (July) 1927.
10. The extract used in the treatment of the patients of this series was supplied by Lederle Laboratories, Inc., of New York, known as Solution Liver Extract Parenteral, N. N. R.
11. Cunningham, T. D.: A Method for the Permanent Staining of Reticulated Red Cells, Arch. Int. Med. **26**: 405 (Oct.) 1920.

October 28. He stated that during this time he had taken 120 Gm. of liver daily, usually cooked. In October the red blood cell level was 4,250,000 (highest level reached) and he was advised to increase his intake to 240 Gm. daily.

In spite of several written requests that he return to the clinic for observation, he did not do so until May, 1931, at which time his blood count was even lower than on the first admission, and there was now definite numbness and tingling of the hands and feet. He had taken no liver for four months.

He was again admitted to the hospital, and on four successive days (May 17, 18, 19 and 20) received intravenous injections (20 cc. each) of an extract prepared from 100 Gm. of liver. Each injection was followed in about one hour by a chill of moderate severity lasting for twenty or thirty minutes and accompanied by a rise in temperature. No liver or extract was given by mouth until June 9, when the daily ingestion of 300 Gm. of raw liver pulp was started.

Figures showing the response of the blood to each form of treatment in this patient are shown in charts 1 and 2.

These charts show that the extract prepared from 400 Gm. of liver injected intravenously produced a definitely greater number of reticulocytes and a more marked increase in a similar period of time than was produced by means of the daily ingestion of 300 Gm. of liver. There was also a greater increase in red blood cells, following the intravenous use of liver extract, during a slightly shorter period of hospitalization, and at the end of one month after discharge from the hospital the highest blood level as yet attained by this patient was reached. At this time the patient's general condition was excellent and there was practically no numbness and tingling of the hands or feet.

Another patient, a man, aged 43, entered the hospital in June, 1931, with definite symptoms of only two months' duration and with a typical picture of pernicious anemia. The red blood cell count was then 1 million red cells per cubic millimeter of blood. His chief complaints were anorexia and nausea with vomiting. In consequence it was difficult for him to retain food. At noon of June 8 he was given intravenously extract prepared from 50 Gm. of liver. At 1 p. m. on the following day he received extract from 20 Gm. of liver, and at 6 p. m. of the third day extract from approximately 80 Gm. of liver. Each injection

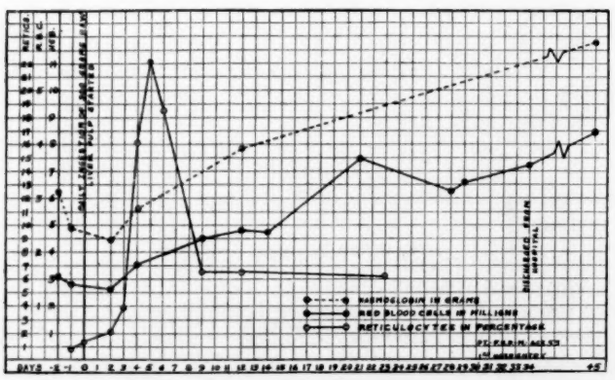

Chart 1.—Effect of the daily ingestion of 300 Gm. of raw liver pulp on the blood of patient F. H. P. in first relapse, for comparison with chart 2. The perpendicular heavy black line to the left indicates the day on which liver treatment was started. In this chart and the others shown here the day on which treatment was begun is indicated as 0 day, the numbers thereafter indicating days after the beginning of treatment. The bent line indicates a lapse of time greater than that previously indicated in the chart.

was followed in about one hour by a chill, slight nausea and a rise in temperature. The greatest rise occurred after the second or smallest injection. The highest temperature reached after each injection was, respectively, 101, 101.8 and 101 F. No liver treatment was given thereafter until, beginning on the morning of June 22, he received in a period of twenty-four hours three intramuscular injections of a similar extract, each prepared from 100 Gm. of liver, and on August 8 he was started on a daily regimen of 300 Gm. of raw liver pulp by mouth, to be continued after his discharge from the hospital. Clinical improvement kept pace with the improvement in the blood condition, figures for which are shown in chart 3.

The third patient to receive liver extract intravenously was a housewife, aged 55, who entered the private ward in April, 1931. The chief complaints, beginning about six weeks before admis-

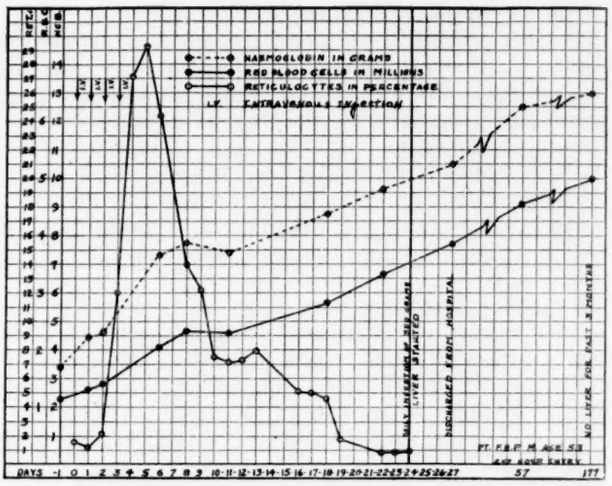

Chart 2.—Effect of liver extract administered intravenously on the blood of patient F. H. P. during a second relapse, to be compared with chart 1. Four injections were given on four successive days, as indicated by the arrows. Each arrow indicates an injection of extract prepared from 100 Gm. of liver.

sion, were numbness and tingling of the fingers with difficulty in holding small objects. April 29, the daily ingestion of 200 Gm. of raw liver pulp was started. This was continued until her discharge from the hospital, May 7. Although the reticulocytes showed an increase from 0.6 to 3.0 per cent, the red blood cell count changed little—from 3.17 million at the time of admission to 3.28 million at the time of discharge. For two weeks thereafter she ingested liver extract from 600 Gm. of liver and for two weeks more extract from 300 Gm. of liver. June 5, the red blood cell count was only 3.4 millions and she was readmitted for further treatment. The daily ingestion of 250 Gm. of liver was started and on June 6 an intramuscular injection of extract prepared from 100 Gm. of liver was given. Because of some pain after this injection, the extract in the same amount was given intravenously on June 12, 16, 19 and 27 and July 1. Again a moderate reticulocyte rise occurred, reaching a peak of 3.9 per cent, and up to the time of discharge on July 1 the red blood cell count had reached a level of 4.63 million cells per cubic millimeter. Numbness and tingling had practically disappeared, and it was possible for her to use her hands in an essentially normal manner.

INTRASPINAL TREATMENT WITH PATIENT'S SERUM AFTER INTRAVENOUS LIVER EXTRACT

The fourth patient to receive intravenous treatment also received intraspinal injections of her own serum after the intravenous injection of liver extract:

A woman, aged 63, had noticed tingling of the hands and feet for about four years, together with coldness of the legs and a tendency to stub the right toe. The symptoms had increased in intensity and it became impossible for her to retain small objects in either hand or to recognize them by feeling with the right. The gastric contents contained no free hydrochloric acid and a low total acidity by a fractional Ewald meal and histamine. The red blood cell count was not markedly reduced below normal (4.2 million), although the individual cell volume (9.4×10^{-11})[12] was greater than the normal. The basal metabolic rate was plus 13 per cent. A few weeks before admission

12. Murphy, W. P., and Fitzhugh, Greene: Red Blood Cell Size in Anemia: Its Value in Differential Diagnosis, Arch. Int. Med. **46**: 440 (Sept.) 1930.

to the hospital the vibration of a tuning fork was barely detected over the left tibia and not at all over the right. On admission to the hospital, vibration sense was absent over both tibias.

Effect of Intramuscular Injections of Liver Extract *

Case	Sex†	Age	Red Blood Cells, Millions	Hemoglobin, Gm.	Days After Treatment	Reticulocytes, per Cent	Intramuscular Injections: Day Given	Intramuscular Injections: Amount per Dose
1	♀	58	1.82	7.73	0	1.1	1.....	200 Gm.
			2.17	8.14	4	13.5	2.....	150 Gm.
			3.37	.....	14	5.1	Daily there-	10 Gm.
			3.87	10.07	22	1.8	after	
2	♀	68	2.38	9.52	0	0.4	1 and 11.....	300 Gm.
			2.12	7.04	4	8.5	20.....	200 Gm.
			3.68	10.19	25			
3	♂	65	1.51	6.50	0	1.2	1.....	300 Gm.
					4	13.8		
			3.35	10.63	18			
4	♂	65	2.45	11.04	0	1.6	1, 2, 6, 9.....	100 Gm.
			3.22	11.32	4	7.3	11 and 16....	First intravenous
			4.03	13.80	16			
5	♀	63	2.76	10.21	0	0.6	"Aolan" 1...	1 cc.
			2.92	10.07	4	0.6	"Aolan" 2	4-5 cc.
			3.16	.....	8	0.5	and 3	
			3.64	10.49	14	3.5	Liver extract 8 and 9	100 Gm.
6	♂	57	1.39	5.11	0	0.5	1, 2, 3.....	100 Gm.
			1.82	6.62	4	15.4		
			2.68	8.14	12	4.3		
7	♀	65	2.67	9.66	0	0.6	1, 2, 3.....	100 Gm.
			2.30	10.21	6	2.2		
			3.19	9.25	13	1.7		
8	♂	63	1.00	4.28	0	0.8	2 doses 1....	100 Gm.
			1.33	4.00	5	28.0	2 doses 2....	100 Gm.
			2.84	8.28	13	4.7	(at 12 hour	
			4.12	10.76	26		intervals)	
			4.53	11.59	34			
			5.01	12.70	62			
9	♀	43	2.10	8.58	0	0.9	1.....	200 Gm.
			1.84	.....	3	17.4	31.....	100 Gm.
			2.70	9.36	12	3.9		
			3.63	9.72	27			
			4.28	10.49	34			
10	♀	59	3.48	9.48	0	...	1, 3, 9, 13, 20,	100 Gm.
			3.65	13.25	6	4.1	27, 34, 41	
			4.04	14.08	13	0.6		
			4.36	.....	20			
			5.12	14.90	41			
11	♂	58	2.94	12.70	0	1.3	1 every 7	100 Gm.
			3.31	13.11	9	2.5	days	
			3.85	11.85	13			
			4.54	13.52	34			
			4.67	13.25	41			
			4.84	14.16	48			
			5.14	14.57	55			
12	♂	55	3.79	11.18	0	....	1 every 7	100 Gm.
			3.52	13.80	7		days for	
			4.27	11.59	14		6 doses	
			4.59	14.21	42			
			4.89	14.00	102			
13	♀	59	3.58	10.27	0	....	1 every 7	100 Gm.
			4.19	11.06	7		days for 7	
			4.37	11.85	21		doses, and	
			4.50	12.60	42		Extract by	300 Gm. daily
			5.03	13.76	76		mouth	
14	♀	70	3.85	11.06	0	....	1 every 7 days	100 Gm.
			3.99	11.06	7		for 7 doses	
			4.58	12.64	21		Extract by	200 Gm. daily
			4.84	12.64	42		mouth	
			5.07	12.64	80		Liver by mouth	120 Gm. fried
15	♀	56	4.43	10.92	0	....	1 every 5	100 Gm.
			4.30	10.90	8		days for	
			4.96	11.70	28		8 doses	
			4.98	12.48	42			
			5.05	12.49	71			
16	♂	65	4.45	12.04	0	....	1 every 5	100 Gm.
			4.11	12.90	7		days for	
			4.60	13.05	18		8 doses	
			4.18	13.88	38			
17	♀	65	4.49	12.04	0	....	8 in first 33	100 Gm.
			4.77	13.76	20		days	
			5.06	13.76	33		8 in last 24 d.	100 Gm.
			4.52	12.90	79		33d to 79th	300 Gm. daily
			4.58	13.88	93		day, extract	
			5.20	13.86	103		by mouth	

* In the first seven cases recorded, the type of treatment was changed after intervals varying from twelve to twenty-five days and the figures are here recorded only up to that time. In the column headed "Days after Treatment," zero (0) day indicates the day of the first injection.

† In this column, ♂ indicates male; ♀, female.

There were marked arthritic changes present in the joints of the fingers and pain probably of arthritic origin in the back and legs, with considerable stiffness of the muscles of the legs and back.

Although there is room for question as to the diagnosis, it is very probable that pernicious anemia with combined sclerosis of the spinal cord is present, complicated by chronic arthritis.

After admission to the hospital the patient was given eight weekly intravenous injections of liver extract prepared from 100 Gm. of liver. Following every other injection, blood was withdrawn and the serum obtained from this was treated as for the Swift-Ellis treatments in tabes dorsalis. On the day following each of four of the intravenous injections, from 15 to 20 cc. of spinal fluid was withdrawn by lumbar puncture and replaced by an equal amount of the serum. Each intravenous treatment was followed by a moderate elevation of pulse and temperature, but no chill occurred. There was some stiffness of the back and moderate pain in the legs after the intraspinal injections, although there were no other unpleasant symptoms. Improvement in the blood was slow, the red blood cell count being normal (above 5 million cells per cubic millimeter) at the end of three months after the first injection. Improvement in the symptoms probably due to the spinal cord sclerosis occurred little if at all during the period of treatment; but when the patient was last seen, four months after the first treatment, there was evidence of some improvement. The hands were numb, although the patient could then hold and feel objects, locomotion was easier, and although there were still tingling and stiffness in the feet, the feeling as though there were a spring under her feet, to which she ascribed her staggering gait, had totally left her. At this time tuning fork vibration sense was better on the left but still absent over the right tibia.

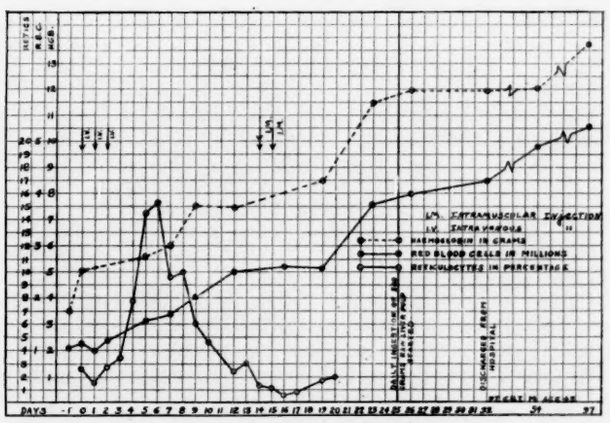

Chart 3.—Effect of an initial minimal dose of parenteral liver extract. Injections were first given intravenously, the arrows to the left indicating three doses of extract prepared from 50, 20 and 80 Gm. of liver, respectively, given on three successive days. Later, as indicated by arrows, three intramuscular injections each from 100 Gm. of liver were given within a period of twenty-four hours. Liver ingestion was started, as indicated by the heavy line toward the right of the chart.

It is very difficult to decide just how much improvement may have occurred in the presence of the complicating arthritis. What little improvement may have occurred may well be the result of improvement in the blood condition due to the intravenous injections. Liver or liver extract by mouth was not used in the treatment of this patient at any time.

One other patient with marked spinal cord involvement received one similar intraspinal injection of serum withdrawn after an intravenous treatment without reaction of note. The treatment was not continued, however, because the patient later developed a pulmonary infection which made it necessary to alter his course of treatment. This patient has been further considered among those who received subcutaneous injections. Further trial of this form of treatment will be carried out.

INTRAMUSCULAR TREATMENT

In the accompanying table are recorded briefly observations made of the changes that occurred in the blood of 17 patients who received intramuscular injections of

liver extract. The extract was administered to the various patients at different intervals of time and in varying amounts. These variations in time and amount are recorded in the table. As several of the patients received intramuscular injections only at the beginning of treatment, the figures in the table show the trend of the blood in these only to the point at which treatment was changed. A detailed discussion of these cases will not be undertaken, as the response to the liver occurred in a satisfactory manner except in two complicated cases which will be discussed further.

Case 1 in the table has been reported in greater detail elsewhere [13] because of a number of interesting features. This patient had a blood picture simulating that seen in pernicious anemia and having the characteristic neural changes of that disease, but with a normal amount of free hydrochloric acid in the stomach contents. A relapse to the level recorded in the table on admission occurred after a remission had been produced with oral treatment with liver extract and during the time that she was ingesting daily the extract prepared from 800 Gm. of liver. Although the response of the blood to intramuscular treatment was good, the patient died while in the hospital from meningitis produced by

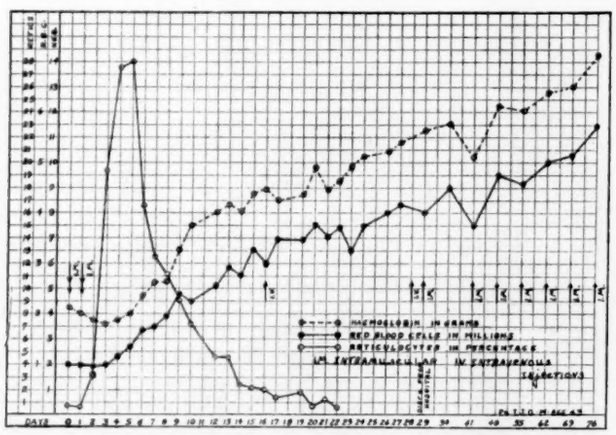

Chart 4.—Effect of an initial optimal dose of extract administered intramuscularly. Each arrow indicates the injection of extract prepared from 100 Gm. of liver. Two of the later injections were given intravenously. Compare the record of reticulocytes with that of chart 5, in which essentially hourly counts of the reticulocytes in the same patient are recorded.

extension from a large trophic ulcer which was present on admission.

Patient 7 entered the hospital shortly after an attack of colic produced by a stone in the bile duct. Three days after the first intramuscular injection of liver extract, another attack of colic occurred. The icteric index of the blood serum was then 15. On the sixth day after the first of three daily injections of 5 cc. of the extract prepared from 100 Gm. of liver, the reticulocytes reached a level of 2.2 per cent, at which time the red blood cell count had fallen to 2.3 million per cubic millimeter from an original level of 2.9 million.

On the following day she was started on the daily ingestion of liver extract prepared from 300 Gm. of liver and of ferrous carbonate (Blaud's pill) 1.8 Gm., or 30 grains. The liver extract intake was doubled after five days in order that an operation might be performed at the earliest possible moment. Seven days after the reticulocytes had reached the level of 2.2 per cent the red blood cell count had risen to 3.19 million, although the hemoglobin level remained unchanged. Eight days later a cholecystectomy was performed and several stones were found. Improvement occurred rapidly and at the end of a month the red blood cell count had risen to 4.29 million cells per cubic millimeter of blood, and the patient had gained weight and felt well. There is a relatively slow response to the ingestion of liver in the presence of disease of the gallbladder, and it is of interest that a reticulocyte rise of even moderate degree did occur following the use of the intramuscular liver extract in the presence of active disease of the gallbladder.

Patient 5 was first given injections of sterilized milk (Aolan) followed by liver extract. This case will be further discussed later in this paper.

Nine of the seventeen cases cited (cases 1 to 9, inclusive) were hospitalized patients in relapse with red blood cell counts below 3 million cells per cubic millimeter when intramuscular treatment was instituted. Treatment of these patients was carried out in the hospital. Intramuscular treatment was generally given either as a single injection or in from two to four injections during a period of from twelve to forty-eight hours, the total amount of extract injected varying from 10 to 20 cc. prepared from 200 to 400 Gm. of liver. Thereafter treatment was carried out as seemed advisable. In some instances, subsequent injections were given at intervals of varying frequency as recorded in the table. Daily smaller injections were continued in only case 1 of this series.

Increases in the numbers of the reticulocytes occurred as early as forty-eight hours after the first injection, whereas the highest level was reached in from three to six days after the first injection. Improvement in the red blood cell count and hemoglobin level has been rapid and progressive in each instance with the exception of case 7, previously discussed. Clinical improvement generally kept pace with the improvement of the blood, definite signs of change having been noted by the patient as early as forty-eight hours after the first injection. Increased appetite has occurred in many instances, often to a more striking degree than in those patients receiving oral treatment. Increases in weight have occurred in most instances during the first few weeks of treatment, and in a few patients this has been rather marked.

The changes in the numbers of reticulocytes, red blood cells and the hemoglobin level occurring after treatment of patient 8 are recorded in more detail in chart 4. A record of the numbers of the reticulocytes counted at intervals of one hour for several days, except for occasional short periods at night, is shown in chart 5. Some idea of the tremendous stimulus to blood formation produced by the injections may be gained from this chart. Of especial interest is the short period of latency in reticulocyte appearance after the injection and the tidelike daily fluctuation in the numbers of reticulocytes.

Two of the seventeen patients who received intramuscular injections (patients 10 and 11) were first seen when the red blood cell counts were relatively little decreased, the counts being 3.48 and 2.94 million cells, respectively, when treatment was begun. Neither had previously received liver treatment, and in both the most disturbing symptoms were those resulting from spinal cord sclerosis. Each received an injection of 5 cc. of extract containing the substance from 100 Gm. of liver at intervals as recorded in the table. The first patient (patient 10) received the first five injections during a period of twenty days in the hospital and thereafter at seven-day intervals in the outpatient department. The

13. Harvey, E. A., and Murphy, W. P.: A Case of Pernicious Anemia with Free Hydrochloric Acid in the Gastric Contents, to be published.

second of these two patients (patient 11) was not admitted to the ward of the hospital but was allowed to continue at his regular work (manual labor) during the time that he received an injection of 5 cc. of extract containing the substance from 100 Gm. of liver at weekly intervals. A reticulocyte rise occurred (counts were done irregularly because of the difficulty of seeing the patient daily), and in eight weeks from the time the first injection was made the red blood cell count and the hemoglobin had both increased to a normal level. During this time the patient's strength rapidly improved, and the staggering gait and inability to maintain a normal balance, which had been his chief concern, had practically disappeared.

The remaining six patients (12 to 17, inclusive) were all taking liver or liver extract previous to the use of intramuscular injections. The daily ingestion of various amounts of liver, liver extract or both had failed to maintain an entirely satisfactory condition of the blood during the preceding year or more. With the exception of case 14, symptoms resulting from spinal cord sclerosis were marked and were not showing satisfactory improvement, whereas in two instances (cases 12 and 16) slow progression was noted. Various complications were present in this group of patients. Patient 12 complained of indigestion and abdominal discomfort with increasing difficulty in taking the liver. Intravenous cholecystograms showed cholelithiasis and cholecystitis. In case 13 there was syphilis, which had not been adequately treated. In case 15, intramuscular treatment was started only after the development of marked spinal cord damage, progressing during a period of more than a year, with occasional attacks of acute cystitis. In case 16 there was chronic prostatitis with retention, and in case 17 there was a basal metabolic rate varying from minus 25 to minus 30 per cent, elevated somewhat with thyroid treatment.

Although it is very possible that even in the presence of the various complications noted improvement in the blood and general condition could have been produced by an increase in the amount of the liver or extract ingested, this was in most of the patients not feasible either because of the expense or because of difficulty in taking it. Each of the six patients was given, therefore, at intervals of from three to seven days an injection of 5 cc. of extract prepared from 100 Gm. of liver. Two of them also received a small amount of extract by mouth; the others received essentially no liver or extract by mouth during the series of injections. It has been customary to give a series of six or eight injections, allowing an interval of from four to six weeks to elapse with return to oral treatment, and then to continue intramuscular treatment again if it seemed advisable. Two of the patients have received injections subsequent to the first series, although it has been noted in several patients of this group that the blood level continued to climb during a period of weeks after the injections were stopped.

With the possible exception of case 16, the blood of the patients showed a gratifying improvement, the level in each instance returning to normal, in some cases a few weeks after the injections were stopped. Symptomatic improvement was also gratifying in each instance. A gain in strength and in general well being was noted uniformly. Improvement in the disturbances resulting from injury to the neural system were marked in most instances even in the short periods of observation recorded. These changes were especially noticeable in cases 12, 13 and 17. Improvement was so prompt and striking in the first two of these cases that it seemed very possible that there was some specific effect on the central nervous system from the liver extract as used intramuscularly. Rapid return of the blood to a more normal state and maintenance in that state must be considered as the most probable cause for the improvement.

SUBCUTANEOUS TREATMENT

Frequent or daily subcutaneous injections of liver extract have been used with larger and less frequent intramuscular or intravenous injections in five patients. Subcutaneous injections only were given to a sixth patient for a period of two weeks, then discontinued because of a local irritation at the site of the injections. As a test for sensitivity, a few subcutaneous injections have been given to several other patients.

Chart 5.—Reticulocytes counted at intervals of approximately one hour for a period of several days. This illustrates particularly well the prompt effect of the extract and the plateau of reticulocyte formation at about the peak level on the fourth and fifth days after treatment was begun. See chart 4 for comparison. The counts were actually made half an hour later than recorded on the chart.

Although this group of patients had ingested fairly large amounts of liver, liver extract or both, they had failed to maintain their blood in a satisfactory condition. Marked sclerosis of the spinal cord was present in all, and in four the motor tract was so badly damaged that locomotion was practically impossible. These four were hospitalized in order to receive the liver extract in this manner.

The total amount of extract injected and the individual injections varied in different patients. Small doses (the extract of from 2 to 4 Gm. of liver) were given, and were increased gradually in an effort to avoid a reaction, until the patient was receiving weekly intramuscular injections of extract prepared from 100 Gm. of liver. Liver and liver extract by mouth was omitted in four cases and reduced in amount in the other two during the course of parenteral treatment.

Although the range of red blood cell counts (from 3.23 to 4.60 million per cubic millimeter) was not very

low when treatment was started, improvement in the blood occurred in each case at a rate comparable to that occurring in the group treated intramuscularly. Three of the patients showed definite clinical improvement, but in the remainder of the group the amount of treatment has been insufficient and the period of observation too short, in view of the marked neural symptoms, to expect definite symptomatic improvement.

The course of the disease in one of the six patients is worthy of further comment:

A housewife, aged 41, was first found to be anemic in 1929. At that time improvement occurred following the ingestion of liver extract. A relapse occurred in December, 1930, through inability to take a proper amount of potent material. Combined sclerosis of the spinal cord progressed rapidly, with loss of weight and strength until she was unable to walk. A transfusion elevated the red blood cell level slightly but produced a reaction which increased her difficulties. Liver, desiccated hog stomach and various liver extracts were tried successively but could not be retained in sufficient amounts to bring about satisfactory improvement. Her physician was advised then to use intramuscular injections of liver extract. June 8, 1931, she was given a water solution of fraction G (Cohn) prepared from 100 Gm. of liver, another the next day from 50 Gm. of liver, and on the third day extract from 200 Gm. of liver. These were followed by fever, nausea and pain at the site of injection. Three days after the last injection there appeared a generalized rash, simulating that seen with measles, and a feeling of faintness with tachycardia. The red blood cell count was then 3.8 million per cubic millimetetr. She then came to Boston, where subcutaneous injections of extract from 4 Gm. of liver was started. The red blood cell count at this time (July 3) was 4 million. The amount of extract injected was increased gradually, so that by the end of a month the material injected intramuscularly represented from 40 to 100 Gm. of liver, with only slight redness and discomfort at the site of the injection. During the first three weeks of treatment a small amount of a liver extract was taken by mouth, but this was discontinued because of constant abdominal distention and distress from gas. After this extract was omitted the abdominal disturbances cleared up rapidly, not to return during a period of observation of two months. Although the red blood cell increase during the first month after admission to the hospital was only approximately 300,000 cells, they steadily increased to a level of approximately 5 million during the next two weeks, where they have since remained.

During the period of treatment described, exercises designed to retrain the paralyzed muscles were carried out under the direction of Dr. Frank R. Ober. Whereas the patient had been unable to walk at all for many weeks before admission to the hospital, at the end of two months of treatment she could walk about with a cane, looked very well, and had none of the distressing abdominal disturbances. Injections of liver extract have been continued in daily subcutaneous small doses and larger intramuscular injections each week.

Certain other features of this case are of interest, some of which help to explain the difficulty in maintaining a normal blood condition. In 1914 a gastric analysis showed the presence of a normal amount of free hydrochloric acid in the gastric contents. Two recent tests have shown none. In 1922 a subtotal thyroidectomy was done because of elevated basal metabolic rate and typical symptoms of hyperthyroidism. Following this she had taken thyroid substance from time to time because of a low basal metabolic rate (minus 30 per cent) and evidence of hypothyroidism. The thyroid substance was tolerated poorly and was omitted at the time of her admission to the hospital because the basal metabolic rate was then minus 12 per cent and remained at an essentially normal level during the two months of observation. Following the onset of marked cord damage the bladder muscles had become paralyzed, with a resulting cystitis which had become acute at intervals since. The bladder did not empty completely at any time, although no acute symptoms occurred during the two months' observation here recorded.

In this patient the parenteral use of liver extract was invaluable as it seems most probable that the results obtained could not have been accomplished by the usual methods of treatment.

USE OF A NEWER EXTRACT

Three patients with pernicious anemia have been treated with intramuscular injections of a newer extract which has several advantages over that used in the case of the other twenty-seven patients of this series. This extract is a clear, amber colored liquid containing little or no protein. Three cubic centimeters contains the effective substance from 100 Gm. of liver, and little discomfort has followed the injection of amounts up to 6 cc. at a single dose. The negligible discomfort following injection and the concentration of the solution favors the use of initial large dosage in a short period of time and at infrequent intervals as maintenance treatment during a remission in the disease.

The effect of this extract compares favorably with that of the extract previously described. The changes in the blood following treatment of two of the patients are recorded in charts 6 and 7. In each patient the intramuscular injections were preceded by two or three small subcutaneous ones as a precautionary measure against reaction.

The first patient received 3 cc. of extract prepared from 100 Gm. of liver on the first morning, and in twenty-four hours two similar injections, making in all the extract from 300 Gm. of liver, with the results recorded in chart 6. Approximately three years previously, this patient received daily by mouth a quantity of a potent liver extract, resulting in an essentially similar improvement in the blood condition.

The second patient (chart 7) received one injection of 6 cc. of extract prepared from 200 Gm. of liver and three hours later a similar injection. In both patients, clinical improvement was rapid and striking. The increase in appetite of the second patient was so striking that the intake of food became almost alarming and was accompanied by a rapid gain of weight.

A third patient, with a high red blood cell level, had a satisfactory reticulocyte and erythrocyte increase following the injection of 6 cc. of extract prepared from 200 Gm. of liver. Several patients have received injections of both types of extract in order to compare the relative amount of discomfort following each. There has been a negligible amount of discomfort following injections of the newer extract.

REACTIONS AND LOCAL DISTURBANCES

Subcutaneous injections generally were given in the upper part of the arms or anterior surface of the thighs. These were often, although not always, accompanied by a slight stinging sensation and rarely by a more severe painful sensation. An erythematous reddening of the skin, which varied in diameter from 1 up to 10 or more centimeters, often appeared at the site of injection a few minutes after it was made and persisted from a few hours to two or three days. The erythematous area was negligible in those patients who had

not previously taken liver and most marked in those who were most resistant to it and who had the greatest difficulty in consuming liver or extract. The discomfort from the injection and the size of the erythematous area generally decreased during the course of treatment. The amount of material injected seems to have had little influence on the size of the erythematous area.

Intracutaneous injections were tried in small doses in two patients. Following a few of these, the skin

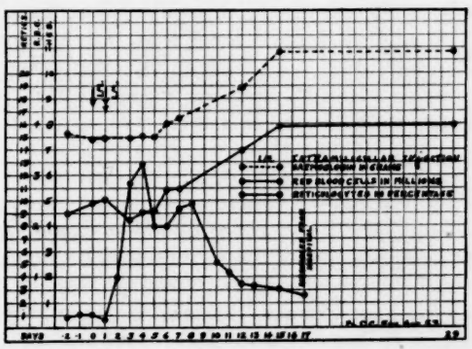

Chart 6.—Effect of injections of the newer type of liver extract used. Each arrow point indicates an intramuscular injection of 3 cc. of extract prepared from 100 Gm. of liver, three doses given within a twenty-four hour period. The failure of the blood to improve between the last two counts is most likely the effect of greater activity on the part of the patient after discharge from the hospital.

became red locally and gradually faded to brown and disappeared, but without sloughing.

The intramuscular injections generally have been given in the gluteal muscles in the customary manner, although occasionally in the trapezii or deltoids. Usually there has been no erythematous reaction about these, although they have been followed often by pain at the site of the injection and down the back of the leg to the ankle, causing stiffness of the leg. The amount of discomfort has varied considerably. In some instances little or no pain has resulted, whereas in other patients and at other times in the same patient the pain has been quite severe and has lasted for from eight to twenty-four hours, occasionally longer. Generally the immediate pain may be lessened or eliminated by first injecting 1 or 2 cc. of a 2 per cent solution of procaine hydrochloride through the injecting needle three or four minutes before the liver extract is injected. Rarely has the discomfort been sufficient so that the patient has been opposed to further treatment by this means. In only three instances has there been a generalized reaction. These occurred after a first injection of extract from 100 Gm. of liver and consisted of a feeling of faintness, palpitation of the heart, and nausea. All these reactions occurred in patients who had been taking liver by mouth. The three patients subsequently have received the injections in small quantities at first, the amount being increased gradually, without subsequent reactions. Because of these reactions, however, it has been my custom to give several daily small injections before giving large amounts in a single dose. Because of the nature of the reactions and because the extract may contain traces of protein, it seems possible that they are allergic phenomena. The occurrence of a marked eosinophilia in an occasional patient treated with liver pulp or extract by mouth suggests sensitization of the patient to the proteins absorbed from the intestinal tract. One patient, who developed an eosinophilia of 55 per cent of 25,400 white blood cells, received subcutaneous and later intramuscular injections of the extract in increasing doses without a reaction. During the period of injection treatment the white blood cell count dropped to 11,800, with 33 per cent of eosinophils.

A rise in temperature above the normal level occurred at times following the intramuscular injections. The febrile reaction was most striking and occurred most frequently when the injections were given during the stage of severe relapse. At these times fever was often present before the injection but increased about one to three hours after it. The highest temperature generally varied between 99 and 102 F. The elevation of temperature resulting from the extract rarely persisted for more than two or three hours, and the fever present during relapse generally was lost in from two to seven days after the onset of treatment. No reactions and essentially no discomfort have been observed following the use of the newer extract.

Following the intravenous injection of the extract there often occurred a generalized reaction in about one hour. This reaction was characterized by a chill of moderate severity, lasting from twenty to thirty minutes, accompanied by a moderate rise in temperature and occasionally by nausea. The reactions were not uniformly present and seemed to be less likely to occur if the patient was kept very warm after the injection. The severity of the reaction was not dependent on the amount of extract administered. The reaction occurred in a similar manner whether or not the patient had previously taken liver or extract by mouth. A more severe type of reaction occurred in only one instance. This patient had taken both liver and liver extract by mouth for several years, although not regularly. He had also received intravenous injections of arsphenamine some years before. These had been discontinued

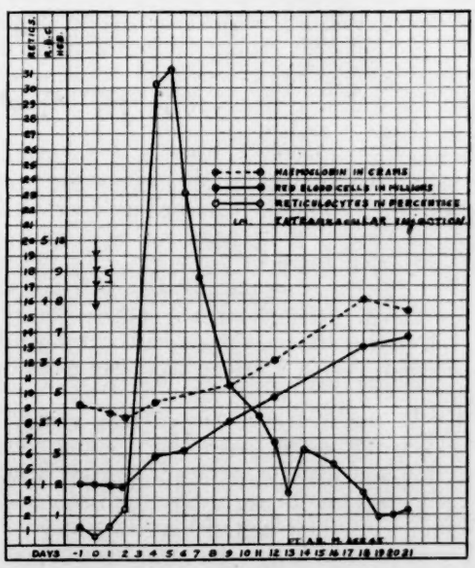

Chart 7.—Changes effected in the blood of a patient who received intramuscular injections of the newer extract used in the case presented in chart 6. Two injections of extract of 6 cc. each prepared from 200 Gm. of liver were given at 10 a. m. and 1 p. m. of the first day of treatment. The injections are represented by the arrows in the chart. The total amount of extract used was prepared from 400 Gm. of liver.

because of reactions characterized by distress and dyspnea with breathing, flushing of the face, and severe pain in the lumbar region of the back. Almost with the first drop of extract put into the vein, flushing of the face was noticed; then a reaction similar to the one described following arsphenamine treatment occurred. The injection was stopped and epinephrine was given, with relief of the symptoms. Only a minute amount

of extract had been given. It was then given subcutaneously in small doses, which were gradually increased until large intramuscular doses were used without further reaction other than that expected locally at the site of injection.

EFFECT ON LEUKOCYTES AND BLOOD PLATELETS

Increase of leukocytes following the ingestion of liver has been noted,[14] the leukocytes generally approaching a normal level during a return to normal of the hemo-

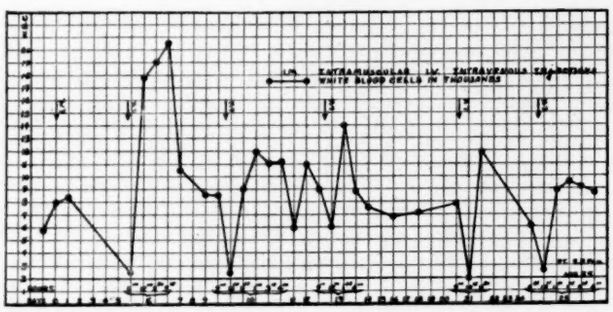

Chart 8.—Effect on the white blood cell count of intravenous injections of extract. Each of the five arrows marked i. v. indicates an intravenous injection of extract prepared from 100 Gm. of liver. Counts of the cells were not made at sufficiently frequent intervals after the first (intramuscular) injection to indicate its effect.

globin and red blood cells. The effect on the leukocytes of the liver extract given parenterally has been so uniformly striking that a somewhat detailed comment on this may be of interest.

The intravenous injection of extract generally caused a temporary depression in the leukocytes about one hour after the injection and at the time of the chill, if one occurred. During the succeeding three to six hours the leukocytes rose to normal or above, tending to remain at a somewhat higher level than they were at the time treatment was started as the general blood condition improved. Typical leukocyte responses are shown in charts 8 and 9.

Intramuscular injections were not followed by a depression in the number of leukocytes but usually by a prompt and marked increase in their numbers, especially of the polymorphonuclear neutrophils during a period of from three to six hours. In twenty-four hours after the injection the number of leukocytes had again decreased, although usually not to the pretreatment level, so that the number of leukocytes had become normal within five to fourteen days after the onset of treatment.

Counts of the platelets showed that a considerable increase occurred within from one to three hours after the injection and that the numbers reached a high normal level within two or three days and so remained.

An example of the effect of liver extract given intramuscularly on the leukocytes and blood platelets is shown in chart 10.

NONSPECIFIC PROTEIN TREATMENT

Owing to the action of the parenteral extract in producing at times a fever and leukocytosis, the question arose as to whether or not the entire effect of the extract was that of a nonspecific protein reaction in spite of the fact that not more than mere traces of protein are present in the extract.

To test this question, a patient was given intramuscular injections of sterilized milk sold under the trade name of "Aolan." On the morning of the first day the patient received 1 cc., on the second day 4 cc., and on the third day 5 cc. Only a slight reaction followed these injections; no increase in the reticulocytes occurred during a period of ten days after the first injection, and there was no significant change in the red blood cell count. On the eighth and ninth days after the first injection of "Aolan," the patient received intramuscular injections of liver extract from 100 Gm. of liver. Practically no effect was noticed by the patient except moderate pain at the site of the injection. The temperature reached a slightly higher level than in the preceding days of observation. In four days' time there was a slight rise in the reticulocytes and a further rise in seven days, when the highest level was observed. During this period of time there was an appreciable increase in the number of red blood cells. This patient is shown as case 5 in the table. Whether or not a greater protein shock would have been more effective cannot be said, and further tests along these lines will be carried out. The results observed suggest, however, that the protein effect of the liver extract is at least a negligible element in producing a remission in pernicious anemia.

Dr. Earle Harvey and I also carried out another test of a slightly different nature. A patient with pernicious anemia was given daily intravenous injections of 30 cc. of normal group 4 blood plasma for a period of ten days. The customary prompt rise in the numbers of the reticulocytes did not occur, although on the eighth day after starting the ingestion of 200 Gm. of raw liver pulp daily there occurred the usual rise.

EFFECT ON THE BLOOD PRESSURE

Frequent observations of the blood pressure were made in some instances following the intravenous injections. No sudden or disturbing change in pressure occurred in any of the patients so observed, although there generally occurred a slight drop in both the systolic and the diastolic pressure during a period of from half an hour to three hours after the injections. A characteristic change is that noted in patient 2, who received intravenous treatment. Before the injection the pressure was 120 systolic and 60 diastolic. At the end of one hour the levels were respectively 115 and 55,

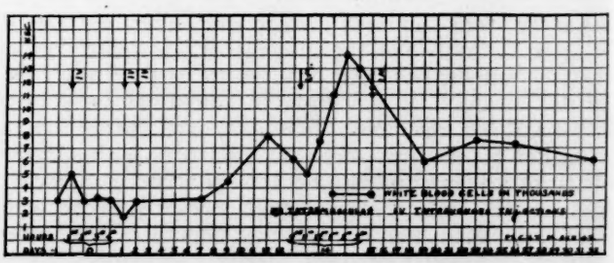

Chart 9.—This chart is similar to chart 8, and the patient is the same as in chart 3. Only a slight drop in count is indicated after the intravenous injection, although sufficient counts were not made to show the actual effect. The increase in white blood cells following the first intramuscular injection is characteristic of that which occurred in many instances. Frequent counts were not made after the last two intramuscular injections.

at which time the chill was occurring. At the end of two hours the pressures were 100 and 45 and in three hours the same.

The pressure generally remained essentially constant during the course of treatment with the extract intramuscularly and over a period of days when given intravenously, except for the slight drop to be explained by rest in bed and adjustment to the surroundings.

14. Murphy, W. P.; Monroe, R. T., and Fitz, Reginald: Changes in Composition of Blood in Pernicious Anemia, J. A. M. A. 88: 1211 (April) 1927.

OPTIMAL AND MAINTENANCE DOSAGE

In an attempt to discover the most satisfactory method of using the parenteral extract, the mode of administration, the dosage, and the interval between injections were varied.

In a recent editorial [15] in THE JOURNAL, caution has been advised in the use of intravenous injections, especially of substances containing protein. Although the extract used in the cases here reported contains little or no protein, the risk entailed in the intravenous as opposed to intramuscular injection must be borne in mind, and as the results obtained in the cases reported show no advantage in the intravenous injections, it would seem advisable to use the intramuscular route of injection generally.

The administration by mouth of optimal amounts of liver or of liver extract at the beginning of treatment as well as during the period of remission has in my experience and in the experience of others given the best results in handling patients with pernicious anemia. The most striking changes in the blood and satisfactory symptomatic improvement has occurred in those patients reported here who have received the larger initial doses of extract, that is, the extract prepared from 400 Gm. of liver during the first two or four days. With the extract now available there is no difficulty in administering such an amount in a single dose or within a period of from twelve to twenty-four hours. Following the initial injection in the patient in relapse with a considerable depression of the red blood cell count, improvement was observed for as long as twenty-nine days without further treatment. It has seemed advisable usually, however, to continue treatment, beginning at from one to three weeks after the first injection. Longer observation of a group of patients will be necessary in order to form any very concise opinion as to the approximate constant dose necessary for the best maintenance of the patient. Although this would seem to be extract derived from 100 Gm. of liver injected at intervals of from five to seven days in resistant cases or in those complicated by severe spinal cord sclerosis and possibly at less frequent intervals (from ten to twenty or more days) in uncomplicated cases, one must determine the maintenance dose for each patient individually by means of careful and prolonged follow-up observations, as has been necessary in treatment by the oral route.

The daily injection of smaller amounts of extract has been received less well by the patients of this series than has the use of larger amounts of extract at less frequent intervals, as the daily use of a needle is generally distasteful to one if it can be avoided. The need for daily injections in order to increase the amount of extract seems to be unnecessary. A short preliminary series in order to insure against a severe reaction or to accustom the patient more gradually to its effect may be advisable in rare instances, although the need for this is doubtful with the newer extract.

EXPENSE OF TREATMENT

The daily and prolonged ingestion of relatively large amounts of liver or of an effective substitute adds a considerable item of expense to the budget of the patient with pernicious anemia. A comparison of the cost of the extract used in some of the patients of this series with that of liver or an effective substitute used orally indicates a considerable difference in the expense. The first patient to receive intravenous therapy was given extract from 400 Gm. of liver, which was sufficient for a period of twenty-four days. The cost of this extract solution is less than $5 ($4.60). On his previous admission he received 300 Gm. of liver daily prepared as the raw pulp. A very conservative estimate of the cost of the liver to the patient not in the hospital would be 30 cents a day, making a total of $7.20 for twenty-four days, or $2.60 more in twenty-four days than the cost of the extract used intravenously, in addition to the effort of preparing the pulp. Were liver extract administered orally to replace the liver for this patient, the substance prepared from 500 to 600 Gm. of liver would have been needed daily. This would entail a daily expenditure of from $1 to $1.50, or $24 to $36 in twenty-four days. The liver extract solution for parenteral use given at seven-day intervals as a maintenance dose would cost $1.15 in that period. A conservative estimate of the cost of treatment with liver by mouth for a similar period would be $2.10, and with extract given orally it would be $4.60. A saving of this degree during a period of a year will amount to a considerable sum and, in view of the advantage in its use to the patient, should popularize the parenteral use of the liver extract solution.

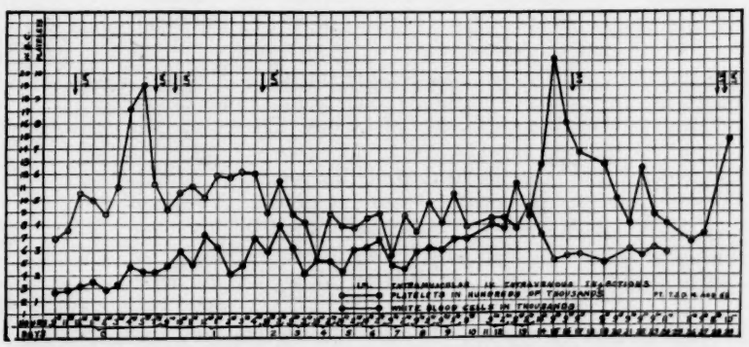

Chart 10.—White blood cells and blood platelets counted at approximately hourly intervals during the day for several days in a patient (see charts 4 and 5) who received intramuscular liver extract. Each arrow indicates the injection of liver extract prepared from 100 Gm. of liver, five intramuscular and two intravenous.

COMMENT

Thirty patients with pernicious anemia have received treatment by means of liver extract administered parenterally. The extract first used for intramuscular injection was a water solution of fraction G (Cohn) prepared in the laboratory at the Peter Bent Brigham Hospital. That first used intravenously and later for intramuscular and subcutaneous injections was prepared with the collaboration of Dr. Guy W. Clark of the Lederle Laboratories and supplied by them for treatment of the patients reported in this series.

The extract is readily available for use and may be administered easily and safely either with or without hospitalization of the patient and with the greatest assurance of success. Improvement in the blood is even more rapid and striking than that to be expected from the ingestion of much larger doses of liver or potent liver extract. Treatment has been followed by an increase in the reticulocytes (young red blood cells) generally within a shorter period than occurs after treatment by mouth, and the numbers of the erythrocytes have increased promptly in practically all cases

15. Safe Products for Parenteral Administration, editorial, J. A. M. A. **97**: 1230 (Oct. 24) 1931.

treated, even in those patients who have been considered to be somewhat resistant to improvement to liver or extract given orally. There has been a prompt and often very striking increase in the numbers of the white blood cells and blood platelets within a few hours of the beginning of treatment and a continuance of a normal or slightly elevated level during the course of treatment. The prompt and often striking increase in the leukocytes and blood platelets suggests the value of the parenteral extract in those diseases in which either of these blood elements are subnormal. As this paper deals with the treatment of the disease pernicious anemia, further comment on the effect of the extract on the leukocytes and blood platelets will be reserved for a subsequent report.

Symptomatic improvement has occurred after parenteral treatment, as is to be expected following the satisfactory oral use of liver or liver extract, although the improvement in general well being of the patient has possibly occurred sooner after the onset of treatment than when oral treatment is used. Improvement in symptoms resulting from the spinal cord damage has been striking in those patients whose treatment has been most satisfactorily carried out. This improvement has occurred usually with a return of the blood count to normal and there is not sufficient evidence to conclude that the improvement has been greater or different than is to be expected following the return of the blood to normal and the instigation of proper exercises for the retraining of the nonfunctioning muscles. Improvement in the neural symptoms has been, however, so prompt and striking in some instances that a "specific effect" of the parenteral extract on these symptoms is suggested. Further observation of this series of patients may answer the question. The data presented following the intraspinal use of "liverized" blood serum is not sufficient to demonstrate its value in the treatment of the neural symptoms and further observations must be made.

The extract has been administered to this series of patients without a reaction of importance. It may be advisable, as has been done in some of the patients with whom this report deals, to test all cases with one or more small preliminary injections in order to avoid the possibility of a severe reaction in the rare patient who may be hypersensitive to the liver.

The experience gained from the treatment of the thirty patients as reported here, together with previously recorded data has led me to the conclusion that the most satisfactory use of parenteral treatment is the intramuscular injection of large or optimal amounts of the liver extract as herein described (extract prepared from 300 to 400 Gm. or more of liver) during the beginning of the treatment of a patient in relapse. Subsequent and maintenance treatment may perhaps best be carried out by similar smaller injections at intervals varying from five to seven days, or even much less frequently in the uncomplicated cases. The exact interval must be determined by the condition of the blood and of the patient. Although the injections may be given daily, such treatment will rarely be indicated, and it has been generally less well received by the patient than treatment at less frequent intervals.

The rapid effect, together with the ease and safety of administration of the extract, especially intramuscularly, makes it an invaluable means of treating the critically ill patient and may well replace the use of either transfusion or stomach tube in the treatment of such a patient. The injection method of treatment should be a valuable substitute for the oral method in the patient who finds difficulty in the constant ingestion of a sufficient amount of liver material or whose gastrointestinal tract is upset thereby, with resultant gas, discomfort or diarrhea. In the latter group the injections may be used permanently or for periods of a few weeks, alternately with liver or extract by mouth. In fact, such an alternation of methods may be desirable during the maintenance treatment of many patients who now find little or no difficulty with the oral regimen.

Finally, mention may again be made of the economy possible through the use of parenteral extract as compared with the expense of either liver or liver extract administered orally.

SUMMARY

Twenty-seven patients who have received treatment by means of a liver extract for parenteral use have been observed.

In four instances, treatment was primarily by intravenous injection, and in seventeen by intramuscular injection. In six, daily smaller subcutaneous injections were also used.

Three other patients received intramuscular injections of a newer, more concentrated extract, which is also more desirable for use than is the extract used in the previously reported twenty-seven cases.

The treatment has led to prompt and striking effects on the blood and the condition of the patients.

311 Beacon Street.

PARENTERAL USE OF LIVER EXTRACT IN TREATMENT OF PERNICIOUS ANEMIA *

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In attempting to identify the material in liver active in the treatment of pernicious anemia, Cohn and his associates [1] and West and Howe [2] have prepared a number of fractions which are found to be potent when injected intravenously into patients with pernicious anemia. In general the use of these fractions on a large scale is not feasible since only a very small amount of active material can be isolated from relatively large amounts of whole liver.

Gänsslen [3] has reported on the intramuscular administration of an extract prepared by pressure from raw liver. He found that the daily intramuscular injection of an amount of this extract derived from 5 Gm. of fresh liver was effective in producing hematologic and clinical improvement in patients with pernicious anemia as well as in patients suffering with other types of anemia. Castle and Taylor [4] have reported a series of three cases of pernicious anemia treated by intravenous injection of a preparation of fraction G [5] in

* From the Department of Medicine, University and Bellevue Hospital Medical College, New York University, and the Third (New York University) Medical Division of Bellevue Hospital.

1. Cohn, E. J.; McMeekin, T. L., and Minot, G. R.: The Nature of the Substance Effective in Pernicious Anemia, Tr. A. Am. Physicians **45**: 343, 1930.
2. West, Randolph; and Howe, Marion: Liver Fractions in Pernicious Anemia, J. Clin. Investigation **9**: 1 (Aug. 20) 1931.
3. Gänsslen, M.: Ein hochwirksamer, injizierbar Leberextrakt, Klin. Wchnschr. **9**: 2099 (Nov. 8) 1930.
4. Castle, W. B., and Taylor, F. H. L.: Intravenous Use of Extract of Liver, J. A. M. A. **96**: 1198 (April 11) 1931.
5. Cohn, E. J.; Minot, G. R.; Fulton, J. F.; Ulrichs, H. F.; Sargent, F. C.; Weare, J. H., and Murphy, W. P.: The Nature of the Material in Liver Effective in Pernicious Anemia, J. Biol. Chem. **74**: lxix (July) 1927.

physiologic solution of sodium chloride. These observers injected the extract derived from 100 Gm. of fresh liver (4.5 Gm. of extract) into two patients and half this amount into the third. In the first two there resulted reticulocyte responses of 27.8 and 25.4 per cent, respectively, and in the third case there was a response of 8.4 per cent reticulocytes. In all cases there followed a rapid increase in the erythrocytes.

Subsequently, Strauss, Taylor and Castle [6] reported on the effects of the daily intramuscular injection of amounts of fraction G, especially prepared, derived from 10 Gm. of liver. It was found that patients treated in this manner showed hematologic and clinical improvement similar to that seen when the intravenous route was used.

It is our purpose in this paper to present hematologic and clinical data showing the effects of the parenteral administration of liver extract in a series of cases of pernicious anemia.

MATERIALS AND METHODS

The diagnosis of pernicious anemia had been made in all the cases included in this study. The patients are divided into two groups: those in active relapse, who were treated in the wards [7] (table 1), and those in remission, who were treated in the hematology subclinic of the General Medical Clinic of the Third (New York University) Division of Bellevue Hospital outpatient department. The latter group will be treated of in some detail later in the section on results and will be designated as outpatients. What follows, therefore, applies only to those patients admitted to the hospital in relapse and studied in the wards. The patients included in this series are not a selected group but represent the first fourteen cases of pernicious anemia that became available while this study was in progress.

Inspection of table 2 shows that the patients may be grouped according to the amount of parenteral liver extract given. The group receiving relatively large amounts of parenteral extract is comparable to that receiving small amounts, in that each group contains patients with very low initial red cell counts, and relatively high counts, patients with and without complications, patients seriously ill and patients only moderately ill, patients with one or more relapses and patients with all degrees of neurologic involvement.

Liver, liver extract and kidney were excluded from the diet during the period of observation. The parenteral extract used was a commercial preparation of fraction G [8] of Cohn, Minot and their co-workers.[5] The extract powder is dissolved in distilled water and heated to 70 C. This solution is filtered through paper, and sufficient sodium hydroxide is added to adjust the p_H to 6.8. It is then passed through a Berkefeld filter, after which it is heated at 80 C. for fifteen minutes. Five cc. of this product represents the material obtained from 100 Gm. of whole fresh liver.[9]

The extract was given intramuscularly, the technic being essentially that of any intramuscular injection. An ordinary all-glass, Luer type 5 or 10 cc. syringe was used with a 20 gage 1 to 1¼ inch needle. The extract was warmed to body temperature. The injections were given into the gluteal muscles, about three minutes being taken for the process. The types of reaction occasioned by this method of treatment will be discussed under results.

The treatment of the ward cases was divided into two periods: initial and subsequent. The initial treatment consisted of one or more intramuscular injections of parenteral liver extract given on successive days. The dose given to each patient is shown in table 2 and is expressed as the number of grams of liver from which the extract was derived. By subsequent treatment is meant all treatment given following the initial treatment. Subsequent treatment was not given until the reticulocytes had completed their increased activity,

TABLE 1.—*Status of Patients on Admission*

Case	Age	Sex*	Total Number of Relapses	Complication Present or Absent	Neurologic Involvement	Previous Recent Treatment	Condition on Admission
1	60	♂	2	Chronic bronchial asthma and emphysema	Slight posterior column changes	None	Severely but not critically ill
2	65	♀	1	None	Very slight	None	Severely but not critically ill
3	65	♂	2	Generalized arteriosclerosis (marked)	.....	None	
4	40	♂	2	None	Slight	None	Uncooperative at time of beginning treatment
5	61	♀	3	None	Slight	None	
6	60	♂	3	None	Marked comb. system disease	¼ to ½ lb. whole liver daily	
7	68	♂	2	None	Well estab. comb. system disease	Small amounts of whole liver	Gradual lapsing due to failure to take sufficient liver
8	58	♂	2	None	Slight	None	Severely ill
9	66	♀	2	None	Slight	Impotent parenteral fraction	
10	63	♀	2	None	Slight	None	Severely ill
11	68	♂	2	None	Slight	None	
12	66	♂	3 or more	Hyperprostatectomy with chronic cystitis	Marked comb. system disease	None	
13	46	♀	1	Low grade cystitis and impacted feces	Marked comb. system disease	None	
14	52	♀	2	None	Very marked comb. system disease	Small amounts of liver extract	Bedridden because of neurologic involvement

* In this column, ♂ denotes male; ♀, female.

until the red cells had reached their maximum following the period of increased peripheral reticulocyte activity, and until the curves of the red cells had remained flat for one week or had continued to fall for one week after reaching their maxima. Subsequent treatment consisted of weekly intramuscular injections of the amount of extract derived from 100 Gm. of liver in all cases except case 4, in which the injections of this amount of material were given at ten day intervals, and in cases 12 and 13, whose subsequent treatment consisted of repeated injections of the extract derived from 25 Gm. of liver at intervals as shown on charts 5 and 6, respectively.

Reticulocyte determinations were made daily during the period of increased peripheral reticulocyte activity, and the hemogram was studied frequently during this

6. Strauss, M. B.; Taylor, F. H. L., and Castle, W. B.: Intramuscular Use of Liver Extract: Maximal Responses of Reticulocytes from Daily Intramuscular Injection of Extract Derived from 10 Gm. of Liver: Preliminary Communication, J. A. M. A. **97**: 313 (Aug. 1) 1931.

7. Cases 1, 3, 5, 6, 9, 12 and 13 were studied in the wards of the Third (New York University) Medical Division; cases 2, 4, 7, 11 and 14 through the courtesy of the First (Columbia) Medical Division, and cases 8 and 10 through the courtesy of the Second (Cornell) Medical Division of Bellevue Hospital.

8. Prepared by the Lederle Antitoxin Laboratories, New York.

9. Solution Liver Extract Parenteral-Lederle, J. A. M. A. **97**: 1077 (Oct. 10) 1931.

period. Red cell and white cell counts were made at least twice weekly. In a small series of cases, during the course of the first few injections, frequent blood pressure readings were taken. Readings were made at sufficiently short intervals, and over a sufficiently long period of time to permit noting any significant change. The patients were closely followed as to their clinical course so that any clinical responses peculiar to this form of treatment might be noted.

RESULTS AND COMMENT

Careful observations were made in all cases to determine the occurrence of any type of reaction to the parenteral injections. The observations were carried on not only during the actual time of injection but for a sufficiently long period afterward, so that delayed reactions might be noted. Specific reactions watched for were the occurrence of pain, local tissue reactions, changes in blood pressure, headache, dizziness or fainting, gastro-intestinal upset such as nausea, vomiting or diarrhea, and various types of allergic or anaphylactic reactions. It may be stated that in practically all cases the patient complained of pain during the course of the injection. As a rule the first injection was the most painful, the severity of the pain seeming to diminish with each subsequent treatment. It seems probable that the explanation for this lies in the fact that the patients became accustomed to the injections. In general the amount of pain varied directly with the size of the dose. Within certain limits, the severity of the pain can be reduced by giving the injections very slowly. As far as can be determined, it would seem that the pain occasioned by injections of parenteral liver extract differs in no respect from that which occurs in other intramuscular injections. It is to be emphasized that the intramuscular injection of liver extract does occasion pain; however, in our series of cases no patient has expressed a desire to forego this treatment because of the pain.

In one patient following the first of a series of intramuscular injections, some induration developed about the site of the injection. This did not go on to suppuration but completely subsided within forty-eight hours. Subsequent injections in this patient produced no untoward reaction, nor did a similar reaction occur in any other patient in this series.

Injections of parenteral liver extract were without significant effect on the blood pressure, observations being made as described under "materials and methods." Headache or dizziness was not encountered in any case, but one patient exhibited mild syncope on two occasions, these being after the first two injections. This patient has since received twenty injections without any repetition of this phenomenon, nor has he experienced any other undesirable reaction. Gastro-intestinal disturbances were not observed in any case. The possible dangers inherent in parenteral medication in general and parenteral liver medication in particular has been called to the attention of the medical profession in a recent editorial[10] in THE JOURNAL. It is perfectly true that parenteral liver extract may produce unpleasant and even alarming reactions when administered intravenously.[4] On the other hand, in our experience of over 500 intramuscular injections given to about fifty patients, the only unfavorable reactions produced were those just described. Specifically, we have never observed paroxysmal dyspnea, cyanosis, pallor or flushing, edema, urticaria or other skin eruptions, chills, or joint pains—allergic manifestations.

RETICULOCYTES

From an inspection of the reticulocyte curves in charts 1 to 6, assuming the upper normal limit of the reticulocytes to be not higher than 2.5 per cent, the meaning of beginning reticulocyte response becomes apparent. Case 10, chart 4, is apparently an exception to this rule, in that the first three reticulocyte estimations were all slightly above the upper limits of normal, although they were at about the same level. It may be seen from table 2 that the beginning reticulocyte response was noted as occurring on the third day in twelve of the fourteen cases. These results are to be compared with those seen following the administration of massive doses of liver extract by mouth.[11] Since reticulocyte determinations were made at twenty-four hour intervals, this means that the beginning response actually took place some time between forty-eight and seventy-two hours. Charts 1 to 6 and table 2 show that the patients were given from one to four injections of parenteral liver extract on successive days during the period of initial treatment. In determining the number of days to beginning reticulocyte response, time is calculated from the day on which the first injection was given. It is apparent from tables 1 and 2 that the time of beginning reticulocyte response did not seem to be influenced by the number of doses given or by the

TABLE 2.—*Initial Treatment and Hematologic Results for Initial Period*

Case	Initial Dosage	Initial Red Blood Cells in Millions	Initial Hemoglobin		Days to Beginning Reticulocyte Response	Days to Reticulocyte Peak	Height of Reticulocyte Peak, per Cent	Final Red Blood Cells, Millions	Final Hemoglobin		Number of Days of Increase
			Per Cent	Gm. per 100 Cc.					Per Cent	Gm. per 100 Cc.	
1	100 Gm. per day for 4 successive days	1.1	18.6	3.2	3	6	36	3.7	47.9	8.1	21
2	100 Gm. per day for 4 successive days	0.9	17.9	3.1	3	7	27	2.9	35.2	6.0	16
3	100 Gm. per day for 4 successive days	1.1	18.8	3.2	3	6	29	2.6	35.5	6.0	11
4	100 Gm. per day for 4 successive days	1.0	20.1	3.4	3	7	24	2.4	38.4	6.6	12
5	100 Gm. per day for 3 successive days	1.3	23.2	4.0	3	6	22	2.9	44.1	7.5	19
6	100 Gm. per day for 3 successive days	2.2	45.8	7.8	3	7	14.8	4.0	67.0	11.4	26
7	100 Gm. per day for 3 successive days	2.4	48.8	8.3	3	5	3.2	3.3	72.9	12.4	22
8	100 Gm. per day for 2 successive days	0.7	14.7	2.5	3	5	31	2.7	36.9	6.9	28*
9	100 Gm. per day for 2 successive days	2.0	42.9	7.3	3	6	19.2	3.0	66.4	11.3	16
10	100 Gm. single injection	0.8	17.2	2.9	3	5	36	2.7	41.8	7.1	15
11	100 Gm. single injection	2.4	59.0	10.0	4	6	8	2.7	58.2	9.9	9
12	25 Gm. single injection	1.9	38.5	6.5	3	7	15.1	3.2	51.7	8.8	14
13	25 Gm. single injection	1.1	21.6	3.7	3	6	19.5	1.7	31.7	5.4	14
14	100 Gm. per day for 23 successive days	2.2	43.5	7.4	5	8	6.5				

* Patient left hospital at own request at this time.

10. Safe Products for Parenteral Administration, editorial, J. A. M. A. **97**: 1230 (Oct. 24) 1931.

11. Riddle, M. C., and Sturgis, C. C.: The Effect of Single Massive Doses of Liver Extract on Patients with Pernicious Anemia, Am. J. M. Sc. **180**: 1 (July) 1930. Connery, J. E., and Goldwater, L. J.: Studies on Patients with Pernicious Anemia Treated with Massive Doses of Liver Extract, ibid. **181**: 609 (May) 1931. Connery, J. E.: Massive Dosage of Liver Extract in Pernicious Anemia, J. A. M. A. **97**: 605 (Aug. 29) 1931. Connery, J. E., and Goldwater, L. J.: Studies on Patients with Pernicious Anemia Treated with Massive Doses of Liver Extract, J. Lab. & Clin. Med., to be published.

size of the doses, by the original level of the red cells, by the presence of complications or by the fact that the patient had been taking some form of liver therapy up to the time of entering the hospital. It would seem from the results obtained (table 2) that in those cases in which several injections were given during the initial period of treatment the reticulocyte response was initiated by the first injection. In the cases studied there was no apparent difference in the time of beginning response between those cases in which the material from 100 Gm. of liver was given in their first dose (cases 1-11, table 2) and those in which the material from 25 Gm. (cases 12 and 13, table 2) was given. The effect of the repeated injections on the time of beginning reticulocyte response becomes a matter for speculation, and it would seem that as far as this particular phase of the reticulocyte response is concerned the second, third and fourth injections had no influence whatever. The rôle of these repeated injections in the subsequent behavior of the reticulocytes and of the red cells will be discussed later.

From table 2 it may be seen that the height of the reticulocyte peak occurred in all cases sometime between the fifth and eighth days, inclusive, calculated from the day on which the first injection was given. Here again, as in the case of "time to beginning reticulocyte response," dosage, initial red cell level, complications, and previous therapy seemed to play no part.

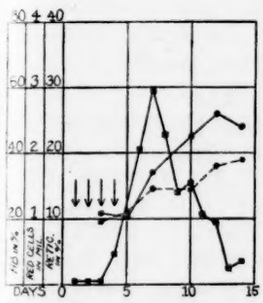

Chart 1 (case 3).—Curves of reticulocytes, red cells and hemoglobin during initial period. In the first six charts the solid line with squares indicates reticulocytes; solid line with circles, red cells; broken line, hemoglobin. Each arrow in charts 1, 2, 3 and 4 indicates injection of parenteral extract from 100 Gm. of liver.

In general, those factors which are regarded as influencing the height of the reticulocyte peak when oral liver therapy is used [12] seemed to operate when the parenteral route was employed. Thus, those cases whose initial red cell level was between 0.5 and 1.5 millions (1, 2, 3, 4, 5, 8, 10 and 13, table 2) all gave reticulocyte peaks greater than 20 per cent, with the single exception of case 13. The fact that a peak of only 19.5 per cent was attained by this patient may have been due either to the presence of complications (table 1) or to the size of the dose given; i. e., the extract from 25 Gm. of liver. A special point of interest in this group is the fact that those cases (8 and 10) in which the material from 200 and 100 Gm. of liver, respectively, was given showed a reticulocyte response of a magnitude comparable to that seen in the patients with similar initial red cell levels who were given the material from 300 or 400 Gm. of liver (cases 1, 2, 3, 4 and 5).

The remaining cases (6, 7, 9, 11, 12 and 14) had one point in common; namely, that the initial red cell counts were within the extremes of 1.9 and 2.4 millions. The height of the reticulocyte peaks in this group varied between 3.2 (case 7) and 19.2 per cent (case 9). Case 6, with an original red cell level of 2.2 millions and a history of previous therapy, reached a reticulocyte peak of 14.8 per cent following treatment with the material from 300 Gm. of liver. In case 14 with a similar initial red cell level and history of previous treatment a peak of only 6.5 per cent reticulocytes occurred, although this patient received the material from 100 Gm. of liver daily for twenty-three days. Both patients had marked combined system disease. Again, patient 12, with an initial red cell count of 1.9 millions, attained a reticulocyte peak of 15.1 per cent following a single injection of the material derived from 25 Gm. of liver in spite of the presence of a complicating hypertrophied prostate and chronic cystitis. In case 9, uncomplicated, with an initial level of 2 millions, the material from 200 Gm. of liver was given and there was a reticulocyte peak of 19.2 per cent, only slightly greater than that of case 12. From these observations it becomes apparent that any generalization, especially attempts to predict reticulocyte responses in the type of case represented by this second group, runs the risk of falling into error.

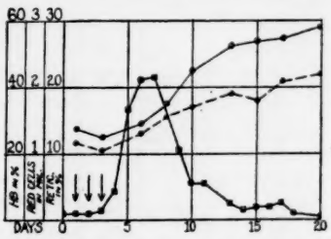

Chart 2 (case 5).—Curves of reticulocytes, red cells and hemoglobin during initial period.

The duration of the period of increased peripheral reticulocyte activity averaged 9.4 days, with extremes of 4 days (cases 7 and 11) and 14 days (case 1).

Patient 12 (chart 5) and patient 13 (chart 6) each received an initial dose of parenteral extract derived from 25 Gm. of liver. Following the initial reticulocyte response, the red cells rose to 3.2 millions in the former and 1.7 millions in the latter. After it had become apparent that no further increase of red cells could be expected as a result of the initial treatment, a second dose of the extract from 25 Gm. was given in each case. There followed in both a second reticulocyte response, reaching a peak of about 6.5 per cent on the third day following the second injection. Because of the fact that the number of reticulocytes had been within normal limits for a period of at least a week, because these second peaks occurred on the third day following the injections, because there had been major peaks of 15.1 and 19.5 per cent twenty-one and eleven days previously, respectively, these second peaks are interpreted as indicating true responses to the second injections and not as "secondary" peaks of the type commonly seen in connection with a major reticulocyte response. The occurrence of these second peaks may be interpreted as meaning either that the original dose given was suboptimal or that the effectiveness of the extract used is enhanced when the parenteral route of administration is employed. In support of the second explanation is the fact that in case 12 the second peak occurred at a time when the level of the red cells was above three million.

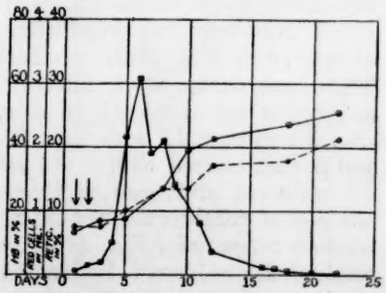

Chart 3 (case 8).—Curves of reticulocytes, red cells and hemoglobin during initial period.

RED CELLS AND HEMOGLOBIN

From an inspection of table 2, it is apparent that no broad generalization concerning the response of the red cells and hemoglobin to parenteral liver therapy can

12. Minot, G. R.; Murphy, W. P., and Stetson, R. P.: The Response of the Reticulocytes to Liver Therapy, Particularly in Pernicious Anemia, Am. J. M. Sc. **175**: 581 (May) 1928.

be drawn from this series of cases. An attempt to divide the series into subgroups on the basis either of dosage or of initial red cell levels results in numbers of cases entirely too small to permit of statistical treatment. There are, however, one or two points that seem worthy of comment. Those cases which showed the highest reticulocyte peaks (cases 1, 2, 3, 4, 5, 8 and 10) all showed large gains in erythrocytes, from 1.4 to 2.6 millions. It is of interest that all these cases presented low initial red counts, the highest being 1.3 millions and the lowest 0.7 million. On the other hand, there was an increase of 2 million red cells in case 6, whose initial red cell count was 2.2 millions, and whose reticulocyte peak was only 14.8 per cent. The discrepancy becomes more apparent than real, however, if reticulocyte concentrations rather than reticulocyte percentages are compared. Again, case 12 with an initial red cell level of 1.9 millions and a reticulocyte peak of 15.1 per cent showed an increase of 1.3 millions, whereas case 13, with a lower initial red cell level (1.1 millions) and a higher reticulocyte peak (19.5 per cent) gained only 0.4 million. Moreover, there was no great difference in the reticulocyte concentrations in these cases at the time of the reticulocyte peaks.

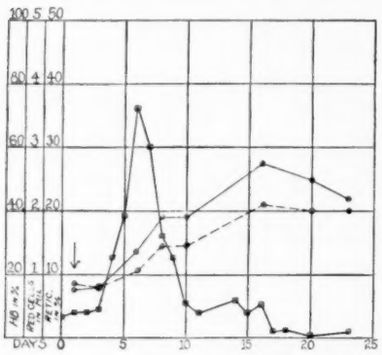

Chart 4 (case 10).—Curves of reticulocytes, red cells and hemoglobin during initial period.

The course of the red cells seems to have been influenced by the duration of the period of increased peripheral reticulocyte activity. In general, those cases in which the period of reticulocyte activity was relatively long showed the greatest increase in red cells, irrespective of the height of the reticulocyte peak, of the initial red cell level, or of the size of the dose given (cases 1, 2, 4, 6, 8, 9 and 10).

The effects of complications on the response of the red cells may be studied in four cases in the series (cases 1, 3, 12 and 13). Naturally no conclusions can be drawn from this small number of cases. The great variation in red cell responses is brought out if case 1 is compared with case 3 and case 12 with case 13. Cases 1 and 3 each started with a red cell count of 1.1 millions, and each received the same amount of parenteral liver extract. Case 1 reached a level of 3.7 millions and case 2 a level of 2.6 millions. Incidentally, in spite of the presence of complications, these two cases showed greater increases in erythrocytes than comparable cases (2 and 4) in which no complications were present. Cases 12 and 13, both with complications and in both of which the same sized dose of extract was given, exhibited entirely dissimilar types of red cell responses. The details of these responses have been given in the preceding paragraph and are shown in table 2.

Qualitative regenerative changes in the erythrocytes were noted in the fixed smears to the greatest degree just preceding or at the time of the greatest reticulocyte activity. These changes became progressively less marked as the period of increased reticulocyte activity drew to a close. Nucleated red cells appeared in small numbers in several of the cases during the period mentioned, but in only two cases (8 and 10) were "blast crises" noted.

With the increase in red cells in response to treatment there also occurred an increase in hemoglobin, with this difference, that the increase in the latter did not keep pace with the former, so that the color index decreased to less than unity. In some cases (1, 2, 3 and 5) the disproportion between red cells and hemoglobin became quite marked. This may have been a function of an early rapid increase in red cells. An idea of what is meant by this early rapid increase in red cells may be gathered from inspection of charts 1, 2, 3 and 4. In some of the cases whose charts are not reproduced here, the increase in red cells during the period of increased peripheral reticulocyte activity was even more striking than in those cases whose charts are given.

From a study of the relationship between dosage and red cell response in this series of cases, several points suggest themselves. For example, in patients receiving the same dose and having similar initial red cell counts, the ultimate red cell levels may show wide variations. Again, cases with different original red cell levels receiving different sized doses may show similar red cell increases. Further, the rapidity with which the red cells increase seems to bear no constant relationship to the size of the dose or to the original red cell level.

WHITE BLOOD CELLS

Significant changes in the white blood cell picture occurred during the period of increased peripheral reticulocyte activity [13] in six cases (2, 3, 4, 7, 8 and 10). Case 7 presented a leukocytosis of 13,000 with no shift to the left of the granulocytes. Case 8 showed a slight leukocytosis but a marked shift to the left. Cases 2 and 3 showed shifts to the left without leukocytosis. In cases 4 and 10 there was a decrease in lymphocytes and increase in granulocytes without leukocytosis or shift to the left. It seems remarkable that this parenteral extract, which is capable of inducing such prompt reticulocyte responses and such early increases in red cells, and which is potent in such small doses, should not have produced more changes in the white cells.

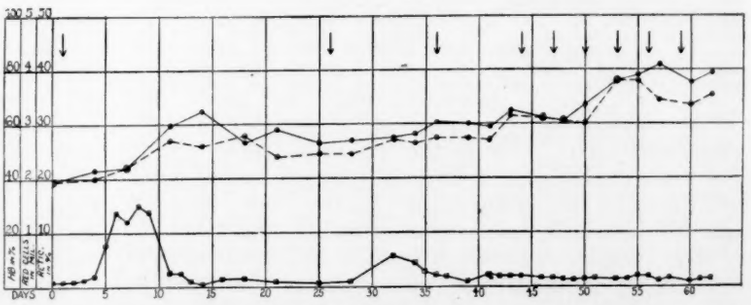

Chart 5 (case 12).—Curves of reticulocytes, red cells and hemoglobin for both initial and subsequent periods. Each arrow indicates injection of parenteral extract from 25 Gm. of liver. Note second reticulocytes increase beginning about third day after second injection.

PLATELETS

The increase in the numbers of platelets was most striking in those cases in which there were blast crises, leukocytosis, with or without a slight shift to the left, or a shift to the left without leukocytosis.

13. Connery and Goldwater (footnote 11). Connery (footnote 11). Minot, Murphy and Stetson (footnote 12).

CLINICAL COURSE

In general, it may be stated that clinical improvement became manifest earlier in the patients treated with parenteral liver extract than is generally observed in patients who are treated with daily doses of liver or liver extract by mouth. The clinical response, however, was no more prompt in these cases than that seen in patients who are treated with single or repeated massive doses of liver extract by mouth.[14]

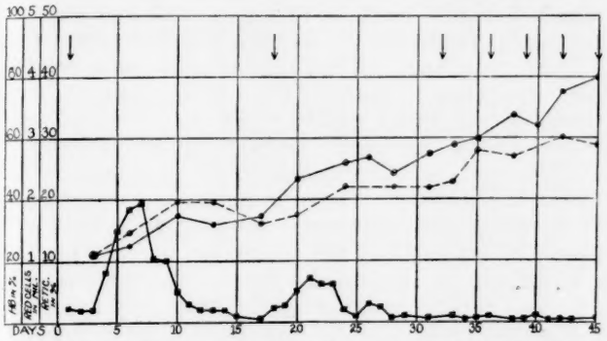

Chart 6 (case 13).—Curves of reticulocytes, red cells and hemoglobin for both initial and subsequent periods. Each arrow indicates injection of parenteral extract from 25 Gm. of liver. Note second reticulocyte increase occurring about three days after second injection.

The clinical course of patients with pernicious anemia who received adequate liver therapy of one sort or another by mouth has been repeatedly described in the literature. Since the nature of the response in the patients who were treated with parenteral liver extract differed qualitatively in no significant way from that of orally treated patients, a detailed account of the clinical course seems unnecessary. As might have been expected, the neurologic manifestations were those most resistant to treatment. The degree of functional impairment dependent on neurologic involvement which is present when the patient first comes under observation may not be taken as an index of what the patient's functional restoration may be after treatment with parenteral extract has been instituted. Patients who may seem at first to be doomed to be permanently bedridden may be so improved that they may be up and about, able to take care of themselves and in some instances gainfully employed. It is not intended to convey the impression that this response is peculiar to parenteral extract therapy or to a regression of the neurologic process, but merely to call attention to the fact that this type of response may occur with this type of therapy.

SUBSEQUENT PERIOD

As was explained under materials and methods, subsequent treatment means all treatment given after the initial treatment and was instituted after the red cells had reached their maxima following the initial treatment and had remained stationary or were decreasing in number for a period of one week. Chart 7 gives the curves of the red cells and hemoglobin during the period of subsequent treatment in cases 3, 5, 8 and 10. These are the cases whose initial period is shown in charts 1, 2, 3 and 4, respectively, and who were selected as being representative of their respective groups. As may be seen from chart 7, subsequent treatment consisted of the parenteral administration of the material derived from 100 Gm. of liver given at weekly intervals. It is apparent that under this treatment there was progressive increase in the red cells and hemoglobin, the increase of the latter not keeping pace with that of the former. Incidentally, if the hemoglobin should persistently remain disproportionately low, one should look for some complicating factor such as bleeding. If this is found, the implication is obvious. Even if bleeding cannot be demonstrated, if the hemoglobin remains low, iron may be used. The patients were usually discharged when the red count had passed the four million level. At the return clinic the weekly injections of the material from 100 Gm. of liver are continued. Thus far, under this regimen, no hematologic or clinical relapse has been encountered, the longest case having been followed for a period of six months. It is not intended to imply that this method of treatment is a complete treatment or the most effective form of liver therapy in all cases of pernicious anemia. Patients who, in spite of a satisfactory hematologic status, develop neurologic changes or show progression of their neurologic lesions while under treatment with parenteral extract should receive supplementary treatment with whole liver by mouth. On the other hand, we have the following: Patient 14 in the present series was admitted with an anemia of only moderate degree but nevertheless was bedridden because of far advanced subacute combined sclerosis. She was treated intensively, receiving the material from 100 Gm. of liver parenterally every day for twenty-three days, and later, the same sized dose two or three times weekly. She remained in the hospital for a period of ten weeks, at the end of which time she was able to be up and about the ward even without the aid of a cane. This is not meant to imply that there was neurologic restoration, for there was no change in the deep reflexes. Acroparesthesias and burning of the tongue were relieved, but what is

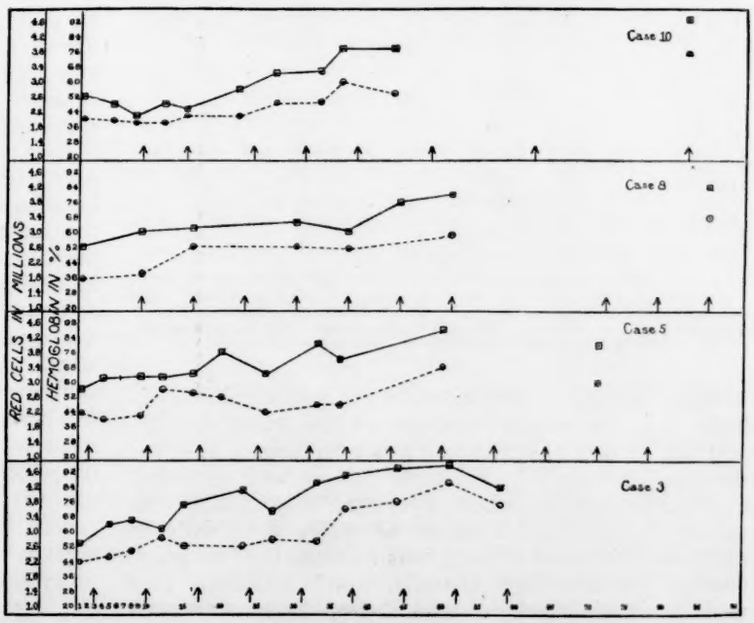

Chart 7.—Curves of red cells (solid line) and hemoglobin (dotted line) for "subsequent period" of cases 3, 5, 8 and 10, whose initial periods are shown in charts 1, 2, 3 and 4, respectively. Time is in days. Each arrow indicates injection of the material from 100 Gm. of liver.

14. Sturgis and Riddle (footnote 11). Connery and Goldwater (footnote 11, second reference. Connery (footnote 11).

more important is that there was no progression of the neurologic process.

At this point it seems appropriate to refer to a group of outpatients who had been receiving other forms of liver therapy at the return clinic and were subsequently changed to parenteral therapy, being given weekly intramuscular injections of the material from 100 Gm. of liver. The data for this group are given in table 3. It is possible that the period during which these patients have been receiving the parenteral extract as the only form of liver therapy is too short to warrant any conclusions and that their clinical and hematologic status may have been maintained as a result of adequate previous treatment. On the other hand E. S. and C. J., table 3, either because of failure to follow the treatment prescribed for them at the clinic or because of the presence of infection, or for some other reason had red cell counts of 3.4 and 3.0 millions, respectively, at the time weekly parenteral treatment was started. Under this treatment they showed progressive increase

TABLE 3.—*Red Cell and Hemoglobin Determinations for Outpatients, Who Had Previously Received Other Forms of Liver Therapy* *

	Case E. S.		Case F. N.		Case F. S.		Case S. S.		Case C. J.	
Date	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin	Red Blood Cells	Hemoglobin
7/14/31	3.41	11.0	....	....	....	....	....	....	....	....
7/21/31	3.64	10.9	....	....	....	....	....	....	....	....
7/28/31	4.27	11.0	4.59	11.9	4.58	10.4	....	....	....	....
8/ 4/31	4.18	11.6	5.28	13.2	4.21	10.8	4.25	11.2	....	....
8/11/31	3.91	11.3	5.05	12.7	4.43	11.1	4.22	10.4	....	....
8/18/31	3.90	....	4.80	....	4.10	....	4.25	....	....	....
8/25/31	4.27	....	4.90	....	3.96	....	4.12	....	....	....
9/ 1/31	5.13	13.6	5.10	15.0	5.44	12.6	4.00	10.8	....	....
9/ 8/31	5.20	12.9	5.08	14.2	4.36	12.1	4.25	10.7	....	....
9/15/31	4.70	11.9	5.03	12.6	4.22	11.6	4.70	10.9	....	....
9/22/31	....	....	....	....	....	....	....	....	....	....
9/29/31	....	....	....	....	....	....	....	....	3.02	10.2
10/ 6/31	4.82	....	5.33	15.0	....	....	....	....	4.02	10.6
10/13/31	....	....	....	....	4.13	13.9	4.16	11.8	....	....
10/20/31	....	....	....	....	....	....	....	....	3.66	12.2
10/27/31	....	....	....	....	....	....	....	....	....	....
11/10/31	....	....	....	....	4.89	14.2	3.82	11.8	4.36	13.4
11/17/31	4.50	13.0	....	....	....	....	....	....	....	....
11/24/31	....	....	....	....	....	....	....	....	....	....
11/28/31	....	....	5.91	....	....	....	....	....	....	....
12/ 1/31	4.54	13.7	....	....	5.16	15.6	4.54	11.2	4.86	14.9
12/ 8/31	....	....	....	....	....	....	....	....	....	....
12/15/31	4.56	14.5	....	....	4.73	14.5	4.20	14.1	....	....

* For details of case F. N. see text under "subsequent period." All patients received weekly injections of the material from 100 Gm. of liver. Red blood cells in millions. Hemoglobin in grams. 100 per cent equals 17 Gm. of hemoglobin per hundred cubic centimeters of blood.

in their red cells. This would argue against the possibility that the weekly injection of the material from 100 Gm. of liver is insufficient as a maintenance dose for the average case. F. N., table 3, had been receiving a large amount of whole liver and a domestic liver extract [15] from half a pound of whole liver daily at the time parenteral therapy was instituted. The progress of his neurologic changes, which had been very rapid in the early stages of his illness, had been arrested by this intensive treatment with whole liver and liver extract by mouth. A short time after parenteral treatment was added to the oral treatment, the patient thought that he was able to walk more steadily and with greater assurance. No changes in his deep reflexes or muscle and joint sense could be detected, so that the feeling of improvement may be largely on a psychic basis. Nevertheless, as shown in table 3, there has been a definite increase in his red cells and hemoglobin, which may afford some basis for the patient's feeling of increased well being.

15. Castle, W. B., and Bowie, M. A.: A Domestic Liver Extract for Use in Pernicious Anemia, J. A. M. A. **92**: 1830 (June 1) 1929.

DOSAGE

The matter of dosage has been discussed in some of its particular relationships in the sections on reticulocytes and red cells. It would seem desirable to add some general considerations concerning the practical use of parenteral liver therapy with particular reference to dosage. The treatment may be given according to one of two plans.

In hospitalized cases in relapse, a series of three or four daily injections of the material from 100 Gm. of liver are given. When the red cells have reached their maximum following this initial treatment, the patient is then given weekly injections of the material from 100 Gm. of liver. In nonhospitalized cases in which it may be inconvenient to do repeated red cell counts, the initial treatment is the same as for hospitalized cases, but treatment is resumed after one week, instead of waiting for the maximum red cell increase as is done in the hospitalized cases. Naturally, if complications should arise during the course of treatment, it is advisable to give the injections more frequently, twice or three times weekly. Likewise, patients in whom complications are present when treatment is started should receive two or three injections weekly after the initial period of treatment. Again, patients having severe neurologic involvement should receive more intensive parenteral liver therapy than those having little or no neurologic involvement (case 14, tables 1 and 2). There are some patients with well established subacute combined sclerosis for whom it may be advisable or even necessary to supplement parenteral liver therapy with the oral administration of whole liver or liver extract or both, in order to prevent progress of the neurologic lesion. There also may be cases in which the advancement of spinal cord changes can be arrested only by large amounts of whole liver taken by mouth. In such cases, parenteral therapy may be a valuable supplement to oral therapy.

It is possible that the dosage recommended here is very much larger than what will eventually be found to be adequate. There is evidence that smaller doses in the initial period may produce results entirely comparable to those obtained from the larger doses (cases 12 and 13). At present it does not seem justifiable to recommend small doses for either the initial or subsequent periods since the number of cases so treated is small, and they have not yet been followed over a sufficiently long period of time.

There are certain problems which arise in the treatment of some cases of pernicious anemia the solution of which seems to lie in the use of the parenteral extract, thus: (*a*) Nausea and vomiting may be so severe that oral administration of any type of liver therapy is out of the question; (*b*) the patient may be unwilling or unable to cooperate in taking oral therapy; (*c*) the patient may be critically ill, so that the time elapsed before beginning response may be an important factor in prognosis; (*d*) the possibility of a patient not taking the prescribed amount of liver or liver extract is obviated; (*e*) a patient may be refractory to oral treatment.

Other situations in which parenteral extract might be used to advantage readily suggest themselves.

After the work of Gänsslen,[3] who reported beneficial results following the use of parenteral liver extract in some anemias other than pernicious anemia, it seemed desirable to ascertain whether or not the extract used in the present study might be effective in the treatment of various types of secondary anemia. With this in mind

a series of seven cases were treated with daily injections of the material from 100 Gm. of liver for four days. The etiologic types of anemia in this series were as follows: nutritional of hypochromic type, two cases; chronic blood loss, one case; malignant condition of sigmoid, one case; aplastic anemia, three cases: chronic benzene poisoning, chronic arsphenamine poisoning, unknown. In none of these cases was there noted any effect on the red cells, hemoglobin, reticulocytes or white cells, nor was there any clinical effect.

SUMMARY

A series of fourteen cases of pernicious anemia in relapse were treated with varying amounts of a parenteral liver extract.

In all the cases there occurred prompt hematologic and clinical improvement.

In general those factors which influence the clinical and hematologic course in patients treated with whole liver or with liver extract by mouth operated in the cases treated parenterally.

A plan of treatment is suggested. There is some evidence that smaller dosage may be adequate.

Nothing in any way suggestive of an allergic reaction of any type was noted in more than 500 intramuscular injections.

A group of cases previously treated with other forms of liver therapy were changed to treatment with weekly intramuscular injections of the material derived from 100 Gm. of liver. Two of these cases showed red cell counts below 4 million when the treatment was changed. All of the cases showed clinical and hematologic improvement, and remained in a state of satisfactory remission during the period of observation.

Special indications for the use of parenteral liver extract are enumerated.

A miscellaneous group of patients suffering with various forms of secondary anemia were treated with parenteral liver extract. In none of these was any hematologic or clinical improvement noted.

75 East Fifty-Fifth Street.

A GRAPHIC REPRESENTATION OF HEMOGLOBIN AND RED BLOOD CELL COUNT RATIOS *

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Few quantitative determinations of blood used in the clinic afford the same opportunity for cross checking of the accuracy of two methods as do the determinations of erythrocytes and of hemoglobin values, since in normal individuals the relationship between these values, usually referred to as the color index (Peters and Van Slyke [1] color: count ratio) is constant. It follows that abnormal color index values are of significance only when it is certain that they are abnormal. In spite of this opportunity for constant checking of data without additional effort, the values for hemoglobin and for color index remain, in most hospitals, only of relative significance, and data accumulated in one clinic, in most instances, cannot be safely compared with data from another clinic. There are two primary reasons for this unsatisfactory condition in regard to unusually important clinical laboratory data. The first reason is the confusion arising from the many hemoglobin "standards"; the second is the error involved in the colorimetric hemoglobin determination with unstandardized apparatus. Both of these errors have been pointed out in previous reviews.

When, in cooperation with the Department of Medicine, the hemoglobin data accumulated by that department in Vanderbilt Hospital were studied, it became evident that the hemoglobin and color index values were erratic and were of significance for the individual patient only when obtained by the same house officer with the same hemoglobinometer. For example, the hemoglobin of one anemic patient was determined by the intern in charge as 50 per cent Sahli on admission. The next day he broke his Sahli tube and borrowed another hemoglobinometer. The hemoglobin of the patient was then 35 per cent Sahli. The red blood count was the same. This represents a 30 per cent error in hemoglobin and color index.

This led us to standardize the method. The medical students and interns use the simple inexpensive Hellige Sahli apparatus with solid glass color tubes. We have had the students of the three upper classes and the interns standardize their hemoglobinometers against blood whose hemoglobin value was determined by the oxygen saturation method with the Van Slyke-Neill gas apparatus. In this standardization a specimen of blood from one of us with a known high hemoglobin value (from 15 to 17 Gm. per hundred cubic centimeters) was obtained and either defibrinated by the Danish technic [2] or oxalated to prevent clotting. This specimen was then divided and placed in bottles containing undiluted blood and in bottles containing blood diluted with 0.9 per cent sodium chloride solution to 75, 50 and 25 per cent of its original hemoglobin content. Each hemoglobinometer was then used in determining, in duplicate, the hemoglobin content of these four samples. In all cases, tenth normal hydrochloric acid was added; fully ten minutes was allowed for development of color, the same hydrochloric acid was used as diluting fluid, and the reading was made with daylight. (When colored screens are used with artificial light, the instrument must be standardized to that light.)

The results were plotted on graph paper (chart 1), and in only two instances was there a deviation from a straight line. This procedure is really equivalent to a standardization with four separate samples of hemoglobin.

The error in these instruments, as is shown in chart 2, was amazing. Many instruments varied over 50 per cent from the indicated value and only a few were accurate. There appears to be no consistent grouping of the error. About twelve of the instruments tested were calibrated in grams by the manufacturer instead of in Sahli units. They were no more accurate than those calibrated in Sahli units and are included in the chart at the proper "percentage error" position. It is important to note that with all but one instrument the error is such that a false high value of hemoglobin is indicated. The instruments were recalibrated and for each a scale reading in grams of hemoglobin was constructed. To answer the question whether or not this simple instrument was capable, if correctly calibrated, of giving satisfactory results, fourteen members of the second year class, chosen because they had had least experience and therefore afforded the severest test,

* From the Department of Biochemistry, Vanderbilt University School of Medicine.

1. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Volume I: Interpretations, Baltimore, Williams & Wilkins Company, 1931.

2. Austin, J. H., and Gram, H. C.: J. Biol. Chem. 59: 535 (April) 1924.

made hemoglobin determination on one specimen of blood, using their own hemoglobinometers standardized by themselves with blood of known hemoglobin content. The results, given in the accompanying table, show that this method is satisfactory for clinical purposes.

The reasons for using absolute units for reporting hemoglobin values have been emphasized again and

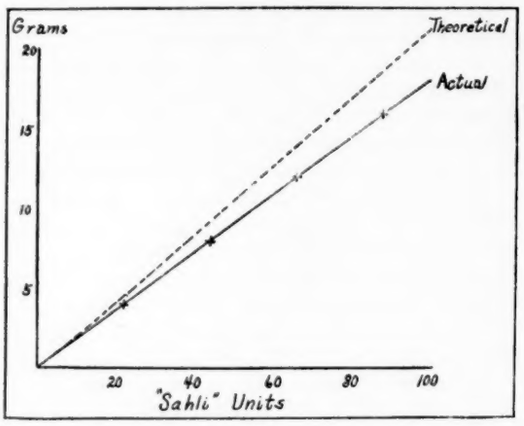

Chart 1.—Sample calibration curve made on a specimen of blood (C. E. C.) containing 16 Gm. of hemoglobin per hundred cubic centimeters. This instrument read 89 Sahli units for 16 Gm., 66.5 for 12 Gm., 44 for 8 Gm. and 22.5 for 4 Gm. The 100 unit ordinate cuts the straight line through this point at 18 Gm., the value used in chart 2.

again, especially by Lindsay, Rice and Selinger,[3] and by Haden,[4] but the custom of reporting in "per cent of normal" on some arbitrary standard still persists

Determination on One Specimen of Blood by Fourteen Students Using Fourteen Hemoglobinometers *

	Gm.
1	14.9
2	14.9
3	15.4
4	16.0
5	15.6
6	15.4
7	15.7
8	15.5
9	15.0
10	15.6
11	15.5
12	14.9
13	15.5
14	15.7
Average	15.4

* The blood contained 15.5 Gm. of hemoglobin per hundred cubic centimeters.

throughout medical literature. There are in existence several Sahli values, the one used being 100 per cent Sahli = 21.25 Gm. of hemoglobin: the Haldane scale, 100 per cent = 13.8; the Haden scale, 100 per cent = 15.6; the Williamson scale, 100 per cent = 16.9, and the Newcomer, 100 per cent = 16.

Almost all other determinations of blood content are reported in some unit per hundred cubic centimeters of blood; e. g., sugar sodium chloride, nonprotein nitrogen and carbon dioxide. Further, in the interpretation of all data of any physiologic variation it is the range of normal variation that is important rather than the average of normal. The necessity of using the same principle for hemoglobin is even greater, since, as shown by Williamson,[5] the normal range for hemoglobin varies with age and with sex. The only question is whether one should use grams of hemoglobin or cubic centimeters of oxygen capacity. Although my colleagues and I have a personal preference for cubic centimeters of oxygen capacity, since, as stated by Peters and Van Slyke,[6] the oxygen capacity is the only accurate means of determining hemoglobin concentration, it was found to be more practical in the clinic to change from per cent of some scale to grams per cent of hemoglobin. Hemoglobin determinations at Vanderbilt are now reported as grams of hemoglobin per hundred cubic centimeters of blood.

The determination and reporting of hemoglobin values having been put on an accurate and logical basis, the next question arose as to what values to use for the normal variation of color index.

It appears more logical and simple to express the hemoglobin content of the red blood cells as "grams hemoglobin in 100 cc. of blood per *one* million red blood cells in one cubic millimeter." The most reliable comparison of red cell count and hemoglobin content, determined by Van Slyke's apparatus, include those of Gram and Norgaard,[7] Haden, Osgood,[8] and Wintrobe and Miller.[9] The values determined by these authors average close to 3 Gm. of hemoglobin in 100 cc. of blood per one million red blood cell count. In view of the slight variations in this value in reports from different laboratories it may be used for clinical purposes as the rounded whole number 3. This whole number factor is as accurate as present data justify, and the dropping of the figures beyond the decimal does away with a false sense of accuracy. The calculation of the color index then is extremely simple, thus:

$$\text{Color index} = \frac{\text{Hb (Gm. per 100 cc.)}}{\text{R. B. C. count (millions per cmm.)} \times 3}$$

Any color index lying between the values 1.1 to 0.9 must be considered within normal variation.

This simple relationship is shown most clearly in chart 3, which is used both for recording hemoglobin and red blood cell values and for calculating color indexes. It is also of value in following the progress of

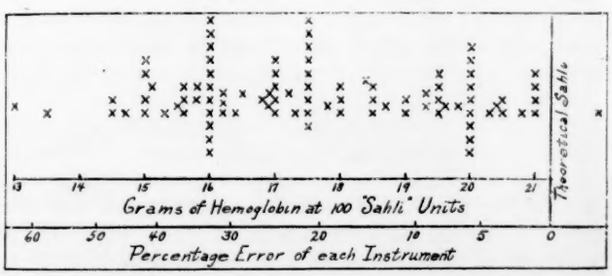

Chart 2.—Variation of a large series of hemoglobin determinations. Each cross indicates the grams of hemoglobin per hundred cubic centimeters which corresponds to the "100 Sahli unit" mark read from the calibrated curve on chart 1. The lower scale gives the percentage error of each instrument; thus, an instrument whose "100 Sahli" mark corresponds to 16 Gm. of hemoglobin would give an apparent hemoglobin value 32.5 per cent too high $\left(\frac{21.25 - 16}{16} \times 100\right)$.

a patient when the successive intersection points of hemoglobin and red blood cell values are numbered and dated.

For any purpose wherein one desires to use oxygen capacity per hundred cubic centimeters, the simple

3. Lindsay, J. W.; Rice, E. C., and Selinger, M. A.: J. Lab. & Clin. Med. **11**: 737 (May) 1926.
4. Haden, R. L.: Accurate Criteria for Differentiating Anemias, Arch. Int. Med. **31**: 766 (May) 1923.
5. Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18**: 505 (Oct.) 1916.
6. Peters and Van Slyke: Quantitative Clinical Chemistry, p. 534.
7. Gram, H. C., and Norgaard, A.: Relation Between Hemoglobin, Cell Count and Cell Volume in the Venous Blood of Normal Human Subjects, Arch. Int. Med. **31**: 164 (Feb.) 1923.
8. Osgood, E. E.: J. Lab. & Clin. Med. **12**: 899 (June) 1927.
9. Wintrobe, M. M., and Miller, M. W.: Normal Blood Determinations in the South, Arch. Int. Med. **43**: 96 (Jan.) 1929.

relation of the rounded number 3 becomes the equally simple rounded number 4 (3×1.34). The calculation then is:

$$\text{Color index} = \frac{\text{Oxygen capacity vol. per cent}}{\text{R. B. C. count (millions per cmm.)} \times 4}$$

This corresponds closely to the value suggested by Peters and Van Slyke,[10] where the value per million equals 3.85. The chart is then easily constructed by using oxygen capacity as ordinate and drawing in the color index lines at any value of red blood cells by multiplying by 4 instead of by 3.

Our experience during the last year has been that the use of these whole number averages of 3 for grams of hemoglobin and 4 for oxygen capacity for each million cells emphasized the clinical significance of the red blood cell count. Haden [11] has shown the value of

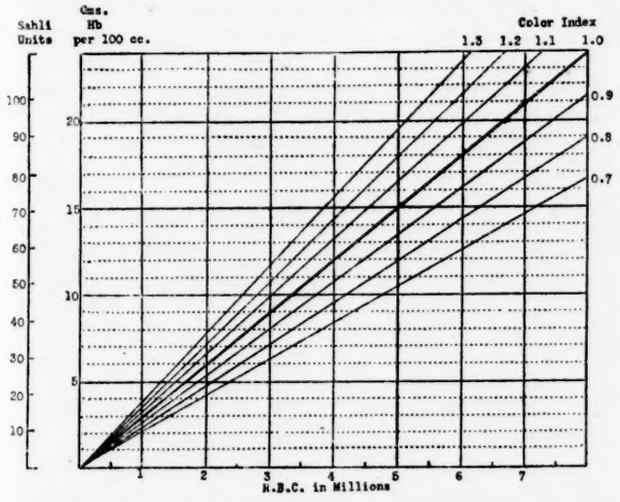

Chart 3.—Hemoglobin and red cell count and color index.

The Normal Range	Adult Men	Adult Women
Red blood cells, millions per cmm.....	4.5–6	4–5
Hemoglobin, grams per 100 cc.....	13.5–18	12–15

The color index indicates whether the hemoglobin content of the erythrocytes being studied is more, equal to or less than normal. The average of the best data indicates that a blood with an erythrocyte count of 5 millions per cubic millimeter contains 15 Gm. of hemoglobin per hundred cubic centimeters; i. e., 1 "million count" = 3 Gm. of hemoglobin then,

$$\text{Color index} = \frac{\text{Hb (Gm. per 100 cc.)}}{\text{R. B. C. count (millions per cmm.)} \times 3}$$

determining the volume index and it would seem that the same principle of recording volume in 100 cc. of blood per one million red blood cells in a cubic millimeter should be used in determining the volume index.

10. Peters and Van Slyke: Quantitative Clinical Chemistry, p. 547.
11. Haden, R. L.: Folia haemat. **31**: 113, 1925.

Cleanliness in Patients with Diabetes.—A diabetic should be the cleanest citizen in the community. His skin is vulnerable. Instead of being filled with glycogen (animal starch), it contains sugar, as Warren, Folin and Trimble have demonstrated. The skin of the untreated diabetic heals slowly, but if the diabetes is under control it heals well. It is because of this wonderful power of insulin to transform sugar, a soluble carbohydrate derived from the food, into glycogen or animal starch, an insoluble carbohydrate, and store it in the skin that the latter is protected. Insulin also stores glycogen in the liver and in the muscles, especially those of the walls of the arteries. Perhaps this deposit of glycogen in the walls of the arteries is of the utmost importance. At least we are hoping that diabetics who use insulin and exercise and diet faithfully will retain more glycogen in the muscular coats of their blood vessels, and that as a result there will be a lessening of arteriosclerosis, which now attacks diabetics prematurely and is responsible for one half of the deaths from the disease.—Joslin, E. P.: Diabetes, Harvard University Press, 1931.

THE VALUE OF LIVER EXTRACT AND IRON IN THE ANEMIA OF YOUNG INFANTS*

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JOSEPH GREENGARD, M.D.
AND
CESSA KLUVER, S.B.
CHICAGO

Anemia in infants, when not secondary to infections, in most cases must be due to a lack of (1) the mineral elements (inorganic elements), (2) the organic element, or (3) the food accessory substances necessary to bring about the utilization of 1 and 2 in the production of red cells and hemoglobin. This lack may be due to a shortage in supplies stored at birth and derived from the mother in utero or from an insufficient available quantity in the diet.

Anemia due to an exclusive milk diet in young animals, "milk anemia," is the form of experimental anemia most easily produced. This anemia in rats and rabbits is due to a lack of sufficient mineral elements in the diet. Steenbock and Hart [1] have shown that iron and copper, the latter in traces only, when added to the milk, prevent or cure milk anemia.

A new-born infant, if born of a healthy mother who had a properly balanced diet during the period of gestation, should have available ample storage of material for forming red cells and hemoglobin to tide it over the period during which it subsists almost solely on milk, Williamson,[2] in a study of the hemoglobin content of the blood at different ages, showed that at birth the normal blood contained 23.5 Gm. of hemoglobin per hundred cubic centimeters. After two and a half days, the hemoglobin content dropped to 23 Gm.; at the age of 6 days, it was 22 Gm.; at 11 days, 21.5 Gm.; at 5 weeks, 18.7 Gm.; and at 4 months, a value of from 13 to 14 Gm. was reached. Approximately this last value is maintained until the second year, when it gradually increases. This work was reported in 1916 and is the largest work on normal hemoglobin. Many of the infants were chosen from private practice; none had ever suffered an infection; they were breast fed, with complemental feedings in some instances.

The material in this study was taken from a home for illegitimate infants. None of the infants received breast milk except two premature infants who received it for two months while they were in incubators at Michael Reese Hospital.

TECHNIC

The blood was obtained from a freely bleeding stab in the infant's heel. All hemoglobin determinations were made by the Fleichel-Meischer method. The instrument was frequently checked by Van Slyke oxygen determinations. The red and white cells were counted in a Bureau of Standards certified counting chamber. The pipets were standardized by us to the same accuracy as the Bureau of Standards certified pipets.

Our purpose in this work was to learn the effect of feeding iron with traces of copper to one group, and liver extract, also with traces of copper, to a second group of these anemic babies. Babies that were gain-

* From the St. Vincent's Infant and Maternity Hospital and the Otho S. A. Sprague Memorial Institute and the Department of Pathology, University of Chicago.

1. Hart, E. B.; Steenbock, Harry; Waddell, J., and Elvehjem, C. A.: Iron in Nutrition: VII. Copper as a Supplement to Iron for Hemoglobin Building in the Rat, J. Biol. Chem. **77**: 797 (May) 1928.
2. Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18**: 505 (Oct.) 1916.

ing weight and appeared quite well except for an anemia were given saccharated ferrous carbonate, 15 grains (1 Gm.), three times daily. Ten such children were in the group (table 1).

The infants who were gaining weight slowly and were in poorer general condition than the group to whom iron alone was given were placed on concentrated liver extract in 20 per cent alcohol, according to

TABLE 1.—*Group of Babies Receiving Iron*

Name	Age Start, Weeks	Period, Weeks	First Count: Hemoglobin, per Cent	First Count: Red Blood Cells, Millions	Last Count: Hemoglobin, per Cent	Last Count: Red Blood Cells, Millions
J. J. M.	6	4	44	3.3	58	3.3
J. J.	8	6	55	3.8	58	3.9
G. F.*†	8	12	57	3.2	100	5.0
J. P.	10	12	59	3.1	82	4.0
L. C.†	16	12	60	3.9	79	4.1
R. S.	16	15	62	4.1	77	4.3
K. F.*	16	16	84	4.5	68	4.5
W. A.	18	15	76	4.0	82	4.6
J. J.*	20	16	72	4.2	74	4.4
R. L.*	22	28	69	3.9	71	4.2

*Children suffering from infection.
† Liver extract fed in addition to iron.

the method devised by Dr. M. T. Hanke in 1927 (and used by Koessler [3] in the treatment of pernicious anemia), 0.5 drachm (2 cc.) three times daily. This group consisted of thirteen babies and is shown in table 2.

Iron was given to four of the babies of the liver extract group, and liver extract was given to two babies of the iron group who had failed to show good improvement on liver extract and iron, respectively, these supplements bringing about improvement in the general condition and in the blood.

Chart 1 shows the effect of adding iron to the food of a baby receiving liver extract, at the time it had reached a maximum improvement from liver extract.

TABLE 2.—*Group of Babies Receiving Liver Extract*

Name	Age Start, Weeks	Period, Weeks	First Count: Hemoglobin, per Cent	First Count: Red Blood Cells, Millions	Last Count: Hemoglobin, per Cent	Last Count: Red Blood Cells, Millions
E. W.	7	19	39	3.2	90	4.6
D. B.	8	16	47	3.8	70	4.2
G. P.	8	18	58	3.8	85	4.4
A. B.†	8	8	54	3.5	65	3.2
R. M. W.	10	28	42	3.0	77	4.2
M. G.	12	8	57	3.5	71	4.1
J. S.*	12	12	46	3.6	68	3.5
M. L.*	16	16	65	3.2	76	4.3
G. M.*	16	12	60	3.6	61	4.0
G. S.*	16	22	63	3.7	83	4.7
R. B.†	18	12	72	4.0	76	4.4
V. K.	18	16	77	4.1	79	4.2
A. S.	24	3	63	3.9	70	4.2

* Iron administered in addition to liver extract because of failure to make a proper gain on liver alone.
† Last counts after acute infections.

Evidently the original storage of iron in the infant's system was exhausted at 6 months and the further stimulation of new red cell formation produced a decrease of hemoglobin but, on the addition of iron, both the hemoglobin and the red cell count continued to improve.

Chart 2 shows the effect of adding liver extract to the diet of an infant that was also receiving iron. After the addition of the liver extract, the hemoglobin and red cell count rose to normal (100 per cent), and have been maintained at this value after the liver and iron were dropped, for the past three months.

Chart 3 shows the weight, hemoglobin and red cell count of the premature infants to whom iron and liver extract were administered simultaneously. During the first and second months, the infants received breast milk, the red blood cell count dropping rapidly from 5 million to 3.3 and 2.8 million, respectively, while the hemoglobin changed from 41 per cent in each to 54 and 46 per cent, respectively. On the iron and liver extract, decided gains were made in hemoglobin, red cells and weights.

The iron group (table 1) varied in age from 6 to 22 weeks at the beginning of the experiment; the final counts were made after feeding periods of from four to twenty-eight weeks. Five infants made from 10 to 35 per cent gain in hemoglobin; three were stationary for no apparent cause, while two others lost hemoglobin during acute infection of the respiratory tract, with cervical adenopathy. Two of the babies with stationary blood pictures made good gains after the administration of liver extract simultaneously with the iron.

The babies receiving liver extract (table 2) varied in age at the onset of the experiment from 7 to 24 weeks. The last counts were made after the extract had been administered for a period of from three to twenty-eight weeks. Seven of the group made gains in hemoglobin

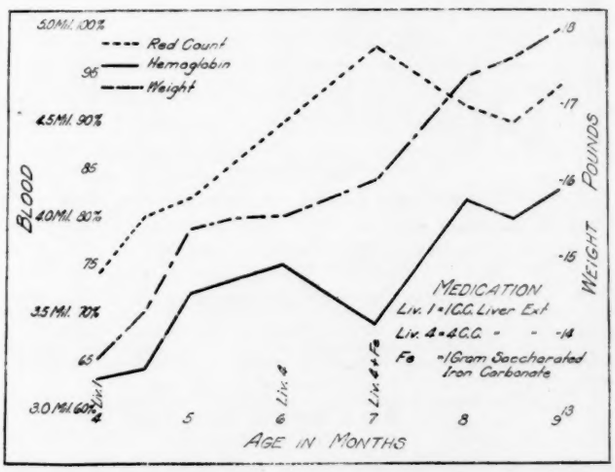

Chart 1.—Effect of liver extract and iron on weight and blood count in an infant (G. S., aged 4 months).

(from 10 to 51 per cent) in from eight to twenty-eight weeks. To three of the infants who had failed to make gains, iron was administered; a fourth, who had made a slight gain in hemoglobin on the liver alone, received iron and made an additional 12 per cent increase in hemoglobin. Two of the three receiving iron made gains of from 11 to 20 per cent, while the third had gained but 6 per cent after the feeding of iron for two weeks.

Liver extract had previously been used by Vascele and by Faber [4] in the treatment of severe anemia in infants, with an excellent gain in red cells and hemoglobin. At that time, it was thought that liver extract was specific for pernicious anemia and that any anemia benefited by it justified one in making a diagnosis of pernicious anemia. Such a conclusion is now known to be unjustified. Griffith and Scott [5] reported six cases

3. Koessler, K. K., and Maurer, Siegfried: The Treatment of Pernicious Anemia with High Caloric Diet, Rich in Vitamins, J. A. M. A. **89**: 768-774 (Sept. 3) 1927.

4. Faber, H. K.: Value of Liver Extract (343) in Identifying and in Treating Certain Anemias of Infancy and of Childhood, Am. J. Dis. Child. **36**: 1121 (Dec.) 1928.

5. Griffith, J. P. C., and Scott, J. P.: Employment of Liver for Anemias of Early Life, M. J. & Rec. **128**: 121 (Aug. 1) 1928.

of anemia in infancy treated with whole scraped liver, from 1 to 2 ounces a day. In two of these cases, good response was obtained. The remaining cases did not show any improvement. The authors discount the results obtained in the two successful cases because other therapeutic measures were also used. They conclude that liver is without much effect in the severe anemias of infancy and that in the mild chlorotic types it offers no advantage over iron therapy.

Herz [6] reported the results of treating a series of infants with powdered liver in doses of from 10 to 25 Gm. a day. Fifteen cases were investigated, in only one of which absolute failure occurred. Two preparations of alcoholic liver extract were tried, both of which were ineffective. The author concludes that anemias in infancy and childhood are very favorably influenced by powdered liver but not by liver extract.

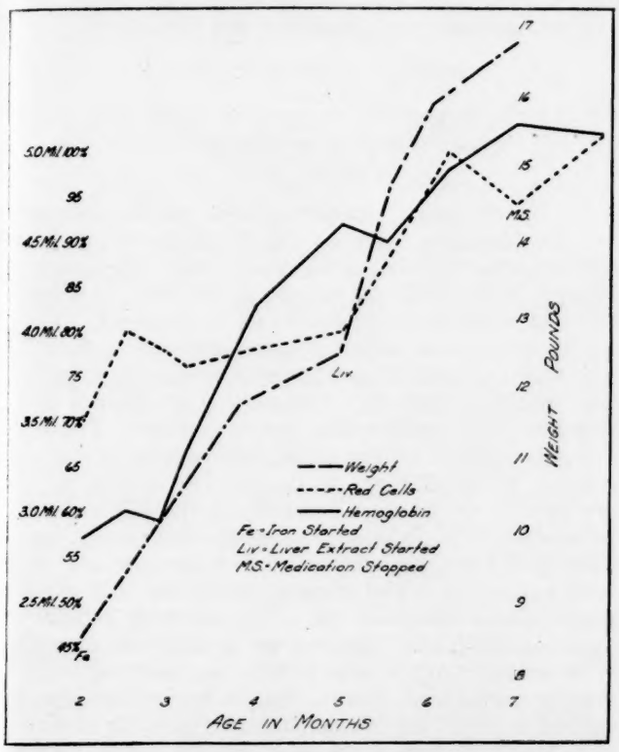

Chart 2.—Effect of liver extract and iron on weight and blood count in an infant (G. F., aged 2 months).

Tuscherer [7] used cooked liver, finely divided, in the treatment of five cases of anemia of infancy. Definite improvement in the blood picture occurred in every case, being manifested usually after three or four weeks of liver therapy. Tuscherer states that there is no doubt that liver therapy brings about improvement, not only in pernicious anemia but in the anemias of infancy as well.

Ligum [8] reported twelve cases of anemia in infancy and childhood, treated with the expressed juice of raw liver. Definite improvement occurred in all cases, but in many of the children gastro-intestinal disturbances frequently developed, with diarrhea.

Lewis [9] reports the use of saccharated ferrous carbonate and copper in the treatment of anemia in infants. In this work, iron was fed for a period of about three weeks, at which time only a small gain in hemoglobin was present. Then copper was fed in addition to the iron and effected a marked gain in hemoglobin. In our series, no copper was administered, as the saccharated ferrous carbonate that we used was believed to contain sufficient quantities of copper as an impurity.

TABLE 3.—*Comparison of Blood of Twelve Anemic Mothers and Their Infants*

	Mother's Blood Near Term			Infant's Blood Day of Birth		
	Hemoglobin	Blood Cells		Hemoglobin	Blood Cells	
		Red	White		Red	White
McC.	88	4.50	13.2	78	5.20	35.0
T.	87	4.40	33.1	81	5.30	33.9
Bl.	80	5.00	5.5	98	5.26	24.0
Br.	76	4.60	16.8	74	4.90	23.5
K.	76	4.60	16.3	86	5.40	24.2
H.	72	4.30	18.0	74	5.10	20.6
F.	72	4.10	13.8	73	4.50	23.1
Tk.	70	3.80	15.5	85	5.28	32.8
Fr.	65	4.20	10.5	78	5.20	35.0
D.	62	4.24	10.5	79	5.52	22.9
McG.	60	3.70	18.6	78	4.72	25.3
M.	47	3.40	11.9	79	4.50	23.1
Average...	71	4.23		80	5.07	

Our chart 2, showing the effect of the late addition of liver extract to the diet of a baby that was receiving iron, practically duplicates the curve of case 4 in Lewis's series.

A comparison of the blood of twelve infants and their mothers, who toward the end of pregnancy or at the time of delivery were found to be anemic, is given in table 3. The average for the group of mothers was 71 per cent hemoglobin, with a maximum of 88 and a minimum of 47 per cent. The new-born infants averaged 80 per cent, but, as they grew older, on artificial feedings this value gradually decreased so that after a few weeks the hemoglobin values were from 60 to 70 per cent of the normal.

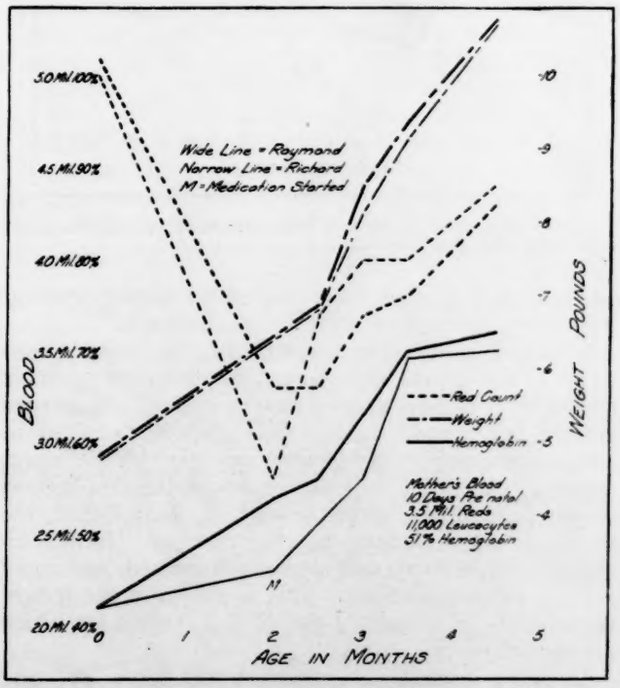

Chart 3.—Effect of liver extract and iron on the blood and weight of premature twins, at the age of 2 months.

6. Herz, Oscar: Leberbehandlung der Säuglingsanämien, Monatschr. f. Kinderh. **40**: 116 (Aug.) 1928.
7. Tuscherer, Jerachmiel: Ueber Lebertherapie bei Säuglinganämien, Monatschr. f. Kinderh. **39**: 264 (June) 1928.
8. Ligum, J.: Liver Therapy of Anemias in Infancy and Childhood, Monatschr. f. Kinderh. **43**: 513 (June) 1928.
9. Lewis, M. S.: Iron and Copper in the Treatment of Anemia in Children, J. A. M. A. **96**: 1135 (April 4) 1931.

That is, speaking in general terms, infants born of anemic mothers have on the average less hemoglobin than Williamson found in those born of mothers with normal blood at delivery. By 2 weeks of age, some already have reached their minimum. The minimum of the normal infant is reached at the age of about 4 months (Williamson).

Chart 4 shows the hemoglobin of the artificially fed infants born of anemic mothers. The hemoglobin percentage is charted, the value found by Williamson for the respective ages being used as 100 per cent. The values are made up by averaging the hemoglobin of different ages of the same groups of infants over the period during which they are receiving the milk as a main source of protein, minerals and vitamin B. Vitamins A and D are administered as cod liver oil, and so on, and vitamin C as orange juice.

It is seen that with the artificially fed infants born of anemic mothers the lowest average value of hemoglobin is reached by the eighth week, while in Williamson's series it was reached in about four and a half months. In our experience the early anemic child is one who is very susceptible to infections and tolerates them poorly. Such infections are accompanied by a decrease in hemoglobin and red cells. These secondary anemias

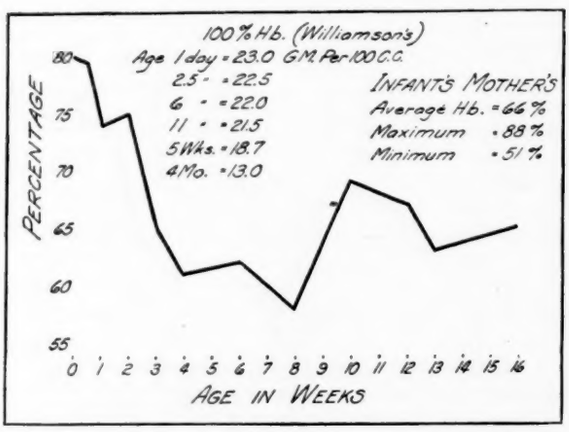

Chart 4.—Average hemoglobin of fifteen infants by weeks, Williamson's value being used as 100 per cent.

are quite slow in improving on artificial feeding, making it harder to maintain a normal rate of growth.

It is well to mention a word about the general condition of the infants who showed improvement on either iron or liver extract or on the two together. Sometimes before, but always by the time the improvement in blood was apparent, the general condition of the infant definitely changed. Appetite improved, the skin became rosier, and normal turgor appeared. In addition, the infants showed definite psychic changes. Irritability disappeared, activity and alertness increased, and rapid gain in weight occurred. This is shown in the weight curves of G. F. (chart 2) and of J. S. (chart 1), which are typical of this series.

In every instance, liver extract was taken well and gastro-intestinal disturbances, such as vomiting or loose stools, were never observed.

CONCLUSIONS

1. It has been found possible to control the anemias of early infancy by administration of liver extract and iron which contains traces of copper.

2. The administration of iron with traces of copper to anemic infants failed to bring about an improvement in blood in about 50 per cent of cases, and liver alone failed in but 37 per cent. The patients in the latter group made significant improvement in blood after iron was added. Also of those infants of the iron series who had failed to make improvements in blood on the iron and copper mixture, those who received liver extract in addition made good gains.

104 South Michigan Avenue.

CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION AND HYPERTROPHY IN YOUNG PERSONS

REPORT OF TWO CASES WITH NECROPSY *

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For many years, primary disease of the coronary arteries (coronary sclerosis) was of interest chiefly to pathologists. In the eighteenth century, Jenner and Parry [1] made a clinical diagnosis of coronary disease and had their diagnosis confirmed at necropsy. Then, for a considerable time, coronary sclerosis with occlusion was thought of as occurring mostly in men and only in elderly persons. Coronary thrombosis is more prevalent among males than among females. The ratio given by various writers varies considerably; some consider it to be as high as 10:1. The disease is not confined to the aged. Commonly in the literature, the terms coronary occlusion, coronary thrombosis, coronary embolism, and myocardial infarction are used interchangeably. The clinical symptoms that accompany acute occlusion of one of the coronary arteries or of one of its main branches are usually characteristic. It is occlusion of the artery, with the resulting infarct, not the method of closure, that is responsible for the cardiac injury. As a rule, it is not possible clinically to be absolutely sure of the exact process that took place; that is, whether the occlusion is due to thrombosis, to embolism, or to both. Then, too, an embolus will often produce occlusion in a vessel that is partially occluded by a thrombus. Occlusion by an embolus, by broken-off vegetation or by a clot from a mural thrombus may occur in younger persons rather than occlusion resulting from pure thrombosis.

Coronary sclerosis with acute and chronic infarction is a vital phase of cardiology, and recently much concerning it has been written. In spite of this, the daily papers continue to contain accounts of persons who have died from so-called acute indigestion, stomach trouble or ptomaine poisoning. Coronary sclerosis with infarction is too likely to be thought of as affecting mostly persons aged 50 years or more. It is no longer a tenable opinion that a person must be at least 40, in order to have fatal occlusion.

Coronary thrombosis with myocardial infarction is relatively rare among persons who are less than 40 years of age, and acute myocardial infarction in young persons is not often given as the cause of cardiac hypertrophy, although our experience, as will appear later in this paper, causes us to think that the two conditions are related.

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* From the Section on Cardiology, the Mayo Clinic.

1. Jenner and Parry, quoted by Wolff, Louis; and White, P. D.: Acute Coronary Occlusion, Boston M. & S. J. **195**: 13-25 (July 1) 1926.

CARDIAC HYPERTROPHY

The exact cause of cardiac hypertrophy continues to be the subject of much interest and discussion. Many theories are given to explain it. Howath [2] explained it on the basis that growth depends primarily on the stretching of muscle fibers. Albrecht [3] was of the opinion that it could be best explained as an inflammatory process. Loeb's [3] theory was that of imbibition of water, with subsequent addition of other materials. Stewart,[4] in his experimental work, showed that hypertrophied cardiac muscle contained slightly more water than did normal muscle. He found also that when myocarditis was produced by injection of epinephrine, the scarred hearts were distinctly hypertrophied and weighed more than the normal in proportion to the body weight.

TABLE 1.—*Reports in Literature of Cases of Coronary Thrombosis with Occlusion in Which Patients Were Aged Forty Years or Less* *

Author	Cases	Age of Patients, Years	Comment
Krumbhaar and Crowell	2	Less than 40	Spontaneous rupture of heart due to coronary disease
Wearn	1	Less than 40	Eighteen other cases reported, mostly in sixth and seventh decades
Parkinson and Bedford	3	Less than 40	Eighty other cases reviewed from standpoint of necropsy
Levine and Tranter	1	39	Patient operated on because of supposed acute abdominal condition; thrombosis of left descending coronary artery found at necropsy
Allan	1	39	Thrombosis of right and left coronary arteries
Kerr, Larkey and Larsen	2	32 and 38	Marked coronary sclerosis with obliteration of lumen in both; thirteen other cases reported
Osler	1	35	Obliteration of left descending coronary artery with sclerosis of anterior portion of left ventricle
Klingman	1	35	Occlusion of right coronary artery, with rupture at base of right ventricle
Palmer	1	36	Marked atheromatous change of coronary arteries, almost with obliteration of left
Nathanson	2	One 32; the other between 30 and 39	One hundred and eleven other cases of occlusion reported
Jamison and Houser	1 1	18	Coronary arteries were tortuous and rigid; right was occluded; subacute appendicitis also present
Clark	1	30	Thrombus in terminal branch of right descending branch of left coronary artery
Dreschfeld	1	12	Severe atheromatous change of coronary arteries
Benda	1	12	Severe sclerosis of left coronary artery with obliteration of circumflex branch
Werley	1	40	Occlusion of anterior descending branch of left coronary artery; acute attack occurred at 25 years of age

* Necropsy was performed in all cases.

Clinically and at necropsy, enlarged hearts are often found without sufficient cause to explain their hypertrophy. It is probable that these cases of idiopathic hypertrophy have led investigators to attempt to explain cardiac hypertrophy on some basis other than that of "work hypertrophy." By work hypertrophy we mean the heart's structural response to the need for more work to maintain the circulation against certain obstacles, such as valvular lesions, pericarditis or severe essential hypertension.

2. Howath, quoted by Stewart, H. A.: The Mode of Action of Adrenalin in the Production of Cardiac Hypertrophy, J. Path. & Bact. **17**: 64-81, 1912.

3. Quoted by MacCallum, W. G.: A Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1924, pp. 480-484.

4. Stewart, H. A.: An Experimental Contribution to the Study of Cardiac Hypertrophy, J. Exper. Med. **13**: 187-209, 1911.

The cardiovascular causes of cardiac hypertrophy are hypertension, rheumatic valvular disease, pericarditis, syphilitic aortitis with aortic insufficiency, myocardial degeneration associated with nephritis, arteriosclerotic heart disease, congenital heart disease and pulmonary obstruction. Other causes are hyperthyroidism, anemia, leukemia, myxedema and idiopathic hypertrophy.

The term work hypertrophy has also been used to mean cardiac enlargement, supposedly caused by increased muscular activity. Whether muscular activity produces cardiac hypertrophy is a much debated question. The term "athletic heart" has gained wide usage. We have never observed a case. The hearts of runners in marathon races have been examined yearly after the annual race at Boston, and they have never shown any evidence of hypertrophy. Crompton [5] stated that six-day bicycle riders showed some evidence of cardiac hypertrophy. Cabot [6] did not find any evidence that the hearts of athletes or of men who had done heavy work during life were any larger than those of people who led sedentary lives.

It has been proved [7] that there is definite correlation between the size of the normal heart and the size of the body; that is, people with large bodies have large hearts, and people with small bodies have small hearts, whether they are active or idle.

SCOPE OF PRESENT STUDY

In this study we have restricted our consideration to cases in which coronary thrombosis with infarction due to primary sclerosis of the coronary arteries was found at necropsy to be the primary cause of death. Coronary occlusion with myocardial infarction is often found associated with other conditions, such as hypertension, nephritis, syphilis, thrombo-angiitis obliterans and certain types of endocarditis. It may also result from an embolus derived from a mural thrombosis. In all these circumstances the infarct may not be large, and often it is not the primary cause of death; other factors are present that may account for the cardiac failure. Excluding cases of hypertension, nephritis, endocarditis, syphilis and thrombo-angiitis obliterans, we were able to find in the literature reports of twenty proved cases [8] of coronary thrombosis affecting patients who were

5. Crompton, quoted by Cabot (footnote 6).

6. Cabot, R. C.: Facts on the Heart, Philadelphia, W. B. Saunders Company, 1926, pp. 421-428.

7. Smith, H. L.: The Relation of the Weight of the Heart to the Weight of the Body and of the Weight of the Heart to Age, Am. Heart J. **4**: 79-93 (Oct.) 1928.

8. These cases were reported by:
Krumbhaar, E. B., and Crowell, C.: Spontaneous Rupture of the Heart, Am. J. M. Sc. **170**: 828-856 (Dec.) 1925.
Wearn, J. T.: Thrombosis of the Coronary Arteries, with Infarction of the Heart, Am. J. M. Sc. **165**: 250-276 (Feb.) 1923.
Parkinson, John; and Bedford, D. E.: Cardiac Infarction and Coronary Thrombosis, Lancet **1**: 4-11 (Jan. 7) 1928.
Levine, S. A., and Tranter, C. L.: Infarction of the Heart Simulating Acute Surgical Abdominal Conditions, Am. J. M. Sc. **155**: 57-66 (Jan.) 1918.
Allan, G. A.: Case Presenting Multiple Arterial Thrombosis Including Both Coronaries, Glasgow M. J. **110**: 351-354 (Dec.) 1928.
Kerr, W. J.; Larkey, S. V., and Larsen, A. E.: Coronary Occlusion and Myocardial Degenerations, California & West. Med. **23**: 46-51 (Jan.) 1925.
Osler, William: Disease of the Coronary Arteries: Fibroid Heart, Tr. Path. Soc. Philadelphia **14**: 106-108, 1887-1889.
Klingmann, Theophil: Spontaneous Rupture of the Heart, New York M. J. **87**: 198-200 (Feb. 1) 1908.
Palmer, W. H.: Spontaneous Rupture of the Heart, with Report of a Case, Boston M. & S. J. **155**: 113-116 (Aug. 2) 1906.
Nathanson, M. H.: Disease of the Coronary Arteries, Am. J. M. Sc. **170**: 240-255 (Aug.) 1925.
Jamison, S. C., and Hauser, G. H.: Angina Pectoris in a Youth of Eighteen, J. A. M. A. **85**: 1398-1399 (Oct. 31) 1925.
Clark, G. F.: Coronary Occlusion: Report of Cases, U. S. Nav. M. Bull. **23**: 487-491 (Dec.) 1925.
Dreshfeld, Julius: On Angina Pectoris and Pseudo-Angina, Practitioner **44**: 28-40 (Jan.) 1890.
Benda, C.: Ueber einen Fall von schwerer infantiler Koronararteriensklerose als Todesursache, Virchows Arch. f. path. Anat. **254**: 600-605, 1925.
Werley, G.: Coronary Infarct and Angina with Abdominal Symptoms, M. J. & Rec. **131**: 367 (April 2), 405 (April 16) 1930.

aged less than 40 (table 1), and about ten cases [9] that we could not include because of insufficient data (table 2).

In the proved cases reported in the literature, the ages of the patients ranged from 12 to 40 years. In the cases in which data were insufficient, the ages ranged from 12 to 39 years. In the reports of these cases there was little mention of cardiac hypertrophy, and in only a few cases were the weights of the hearts given; in the latter cases, the hearts were not particularly enlarged.

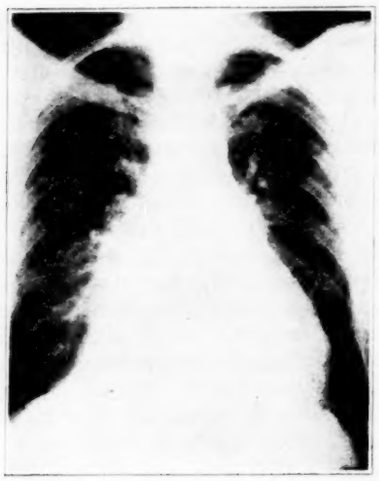

Fig. 1 (case 1).—The heart is enlarged in all diameters.

Most writers have stated that coronary thrombosis is not a cause of cardiac hypertrophy. Few refer to coronary thrombosis with infarction as a cause of cardiac hypertrophy, and none refer to those conditions in young persons. Two cases are reported here, mainly for two reasons: because of the ages of the patients, and because of the marked cardiac hypertrophy which seems to have been secondary to acute myocardial infarction.

The two patients had huge hearts and symptoms of failure, and until death all causes of hypertrophy were excluded, with the exception of pericarditis, which was thought to be the most reasonable diagnosis. The patients gave histories of thoracic pains that were suggestive of acute infarction, but because of their ages and the size of their hearts little consideration was given to the history of attacks of pain. There was nothing in the electrocardiograms that would suggest an infarct. It is believed that the explanation of this is that multiple infarcts were present in both cases. In one case, in addition to the multiple infarcts, there was anomalous distribution of the right coronary artery and an anomalous branch of the left coronary artery.

REPORT OF CASES

CASE 1.—A man, aged 35, came to the Mayo Clinic, March 5, 1931, complaining of shortness of breath. His family history was negative. He had been born in the Netherlands but had lived in western Canada most of his life. He had had the ordinary diseases of childhood, and some type of rheumatism when 8 years of age, but did not have rheumatic fever. He had performed hard farm work without noting any cardiac symptoms until a year and a half before we saw him. At that time, severe pain had developed in the precordial region. This pain had lasted for about twenty-four hours, had been quite steady, and had been made worse by deep breathing. Some relief had been obtained by the application of mustard plasters. The pain gradually had subsided, but soon after this the patient had become short of breath on exertion. About six months later, a similar attack of pain had developed in the same region. Dyspnea had become marked following this attack, and he had been unable to work; finally it had progressed so that he had been able to walk only a short distance without resting. He had not had other thoracic pains than the two severe attacks that have been described. In the few months before his admission he had had considerable palpitation of the heart on exertion; a troublesome cough, worse with exercise, and a yellowish hue to the skin, such that he had been told that he was slightly jaundiced. The blood pressure had never been elevated. One year before he came to the clinic, a roentgenogram of the thorax had given evidence that the heart was not enlarged.

TABLE 2.—*Reports in the Literature of Cases of Probable Coronary Thrombosis with Occlusion in Which Patients Were Aged Forty Years or Less* *

Author	Cases	Age of Patients, Years	Comment
White and Mudd	2	39 and 26	Ninety-three other private cases reported
Stolkind.....	2	One 12; age of other not given	Not Stolkind's cases; the case of patient aged 12 years reported by Wild as an instance of advanced atheroma of coronary arteries; the other reported by Wilks and Moxon as an instance of narrowed obliterated coronary arteries
Sprague.....	1	32	Details not given
Benda.....	2	Both 37	Thirty-nine other cases reported; no details; death due to coronary sclerosis
Wolff and White	1	21	Not Wolff and White's case; they found report in literature; patient was a woman with coronary occlusion
White.....	Not given	Not given	In 62 cases, age ranged from 39 to 82; in 28 recent cases, age ranged from 38 to 80; no reports of cases

* In this group data were insufficient to allow positive diagnosis.

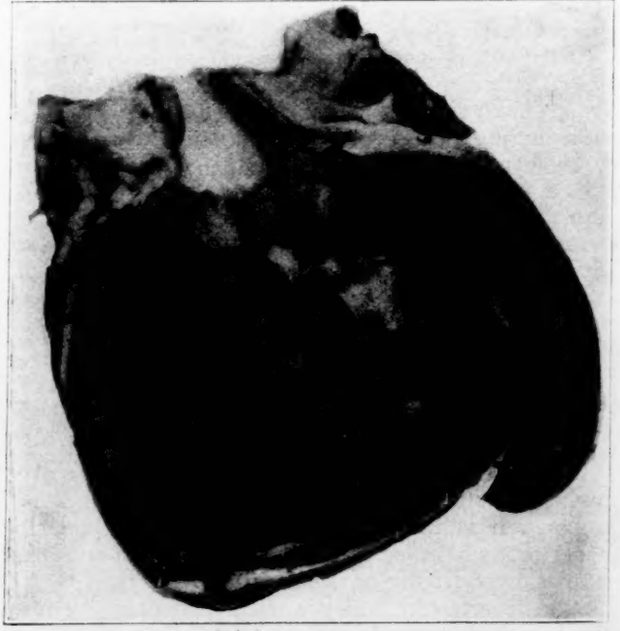

Fig. 2 (case 1).—Extensive chronic infarction of left ventricle; large intramural clot attached to the thinned and sclerotic wall of the markedly dilated left ventricle.

The patient was well developed and fairly well nourished, dyspneic, with slight cyanosis of the lips and nails, and moderately jaundiced. The left border of the heart extended 4 cm. lateral to the nipple line. The tones were poor in quality. There was a systolic murmur, heard over the entire precordial area, but it was not diagnostic. The tones were of poor quality and

9. These cases were reported by:
White, P. D., and Mudd, S. G.: Angina Pectoris in Young People, Am. Heart J. **3**: 1-13 (Oct.) 1927.
Stolkind, E. J.: Angina Pectoris in Children, Brit. J. Child. Dis. **25**: 1-33 (Jan.) 1928.
Sprague, H. S.: Coronary Occlusion, in Nelson: Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1920, pp. 608c-608p.
Benda (footnote 8).
Wolff and White (footnote 1).
White, P. D.: The Prognosis of Angina Pectoris and of Coronary Thrombosis, J. A. M. A. **87**: 1525-1530 (Nov. 6) 1926.

were louder over the base than at the apex. The pulmonic second sound equaled the aortic second sound. There were a few moist râles at the bases of both lungs. The peripheral vessels were not sclerosed more than normal, and examination of the blood, including the Wassermann test, gave negative results. The blood pressure in millimeters of mercury was 120 systolic and 94 diastolic, the pulse rate was 114 beats each minute, and the temperature was 96.7 F. The roentgenographic shadow of the heart was enlarged in all diameters (fig. 1). Roentgenoscopic examination of the heart confirmed this and gave evidence of probable pericardial effusion.

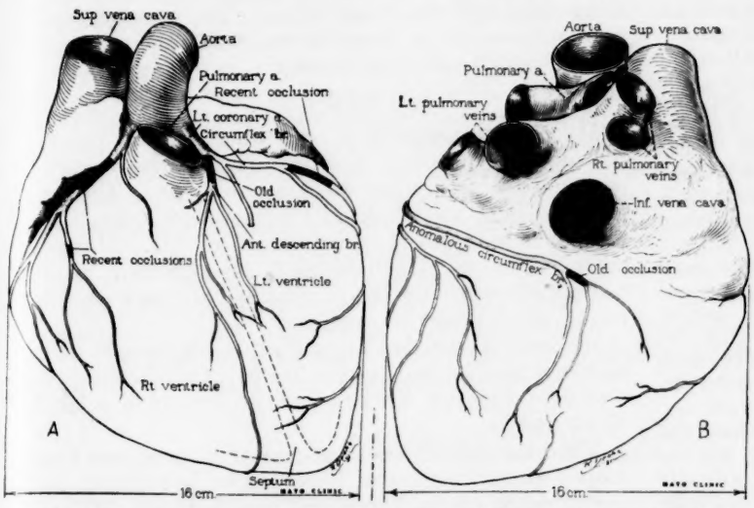

Fig. 3 (case 1).—Sternocostal (*A*) and base and diaphragmatic (*B*) surfaces of the heart, showing the points of occlusion of the coronary arteries in black, and the anomalous circulation. The posterior descending coronary artery arises from the left circumflex artery instead of from the right.

March 7, diagnostic aspiration of the pericardial cavity was performed but fluid was not obtained. The patient was admitted to the hospital following this aspiration. March 14, infarction developed at the base of the right lung. Dyspnea increased, and the general condition grew gradually worse. Some edema and general anasarca developed. Two weeks after admission to the hospital, marked edema of the pharynx and larynx developed, and breathing became stridulous and obstructive. This obstruction to breathing became so marked that emergency tracheotomy was performed, and marked relief was afforded. The jaundice increased, the concentration of bilirubin increased to 14.7 mg. in each 100 cc. of serum, the patient's condition gradually grew worse, and he died suddenly following a severe paroxysm of coughing. When the patient was in the hospital, digitalis, ammonium nitrate and morphine were administered, and mersalyl (salyrgan) was given intravenously, but response to any of these medications was lacking.

At necropsy, the pericardium measured, transversely, 16 cm. and contained 150 cc. of bloody fluid. There were a few fibrinous adhesions to the anterior surface of the left ventricle. The heart weighed 715 Gm. It was pinkish brown and the epicardial fat appeared normal. There was an area 3 by 4 cm. on the anterior surface of the left ventricle, which was covered with adhesions and which corresponded with the region affected by a huge infarct. The wall at the apex of the left ventricle and that of the right ventricle were markedly thinned. The appearance of the opened left ventricle is shown in figure 2. The right ventricle was markedly dilated. There was a large mural thrombus, 9 by 5 by 4 cm., which filled the entire right side of the left ventricle. Around the papillary muscle there were numerous smaller thrombi. In the right ventricle there were a few small mural thrombi at the apex. The valves appeared normal. The papillary muscles of the right ventricle were extremely hypertrophied. In the anterior descending branch of the left coronary artery just below the bifurcation, there was an old occlusion. There was a recent occlusion in the right coronary artery and another in the anomalous circumflex branch of the left coronary artery. These are represented in figure 3. Microscopic study of the vessel disclosed primary intimal thickening without inflammatory change (fig. 4). There were passive congestion of the viscera, and infarcts in the lungs and prostate gland. There was only slight sclerosis of the aorta.

CASE 2.—A man, aged 36, born in Montana, came to the clinic in June, 1929, complaining chiefly of fatigue and dyspnea of six months' duration. His mother had died of heart trouble at the age of 56. His family history otherwise was negative. The patient was a moderate user of alcohol and tobacco. He had had gonorrhea at the age of 25, with a discharge for two months, and he possibly had had scarlet fever. He had been perfectly well until June, 1928, when, after a day's work of carrying baskets of coal weighing from 60 to 75 pounds, he had experienced suddenly severe, tearing, aching pain just below the left nipple. A physician had given medication which had induced sleep. The following day the pain had gone, but the patient had felt exhausted and had remained away from work for a week, after which he had driven a truck without difficulty. In January, 1929, he had noticed the gradual onset of weakness and fatigue, and in February he had been forced to discontinue work because of beginning dyspnea. The dyspnea had progressed to orthopnea. In the two months before his admission, progressive edema had been present and, in addition, many stitchlike pains over the entire cardiac area, especially in the region of the apex, had been noted. One night he had suffered a sudden, stabbing pain in the region of the heart while lying on his left side, but this had not been severe and had subsided by morning. Fever had not appeared in the course of the entire illness.

The patient was wiry, moderately dyspneic and slightly cyanotic. There was an icteric tinge in the sclera. The temperature was 95.8 F. and the pulse rate 104 beats each minute. The transverse diameter of the heart was 20 cm., and the tones were distant but regular. A systolic murmur was present, heard best over the tricuspid area and the apex. The blood pressure in millimeters of mercury was 90 systolic and 86 diastolic. The liver extended 6 cm. below the costal arch and was tender. There was moderate ascites, and edema of the lower extremities was marked.

The concentration of hemoglobin was 85 per cent, and there were 4,620,000 erythrocytes and 10,900 leukocytes in each cubic millimeter of blood. The specific gravity of the urine was 1.010, and it contained numerous hyaline casts, a slight amount of albumin, an occasional erythrocyte and from 8 to 20 leukocytes in each high power microscopic field. The concentration of urea was 122 mg. in each 100 cc. of blood, and creatinine, 2 mg. The Wassermann test of the blood was negative. The eyes were normal except for slight pallor of the fundi. Roentgenologic examination of the thorax showed that the heart measured 20 cm. transversely, and the lungs were clear. The roentgenogram had the same general appearance as that seen in case 1 (fig. 1). The electrocardiogram (fig. 5) disclosed a rate of 92, sinus tachycardia, incomplete bundle branch block (Q-R-S interval, 0.12, 0.14 and

Fig. 4 (case 1).—Apparent complete occlusion of a coronary artery, caused by primary intimal thickening. Some tearing occurred when the vessel was opened.

0.14 second), left ventricular preponderance, and an inverted T wave in lead I, an exaggerated P wave in lead II, and a notched P wave in leads II and III.

The patient was hospitalized in the cardiac service and was given digitalis, mersalyl and ammonium nitrate, without beneficial results. The concentration of urea gradually increased to 195 mg. in each 100 cc. of blood. The dyspnea grew worse, and cyanosis was pronounced. On the sixteenth day after admission, the patient complained of a severe pain in the upper portion of the abdomen, which was projected up over the heart; this was of twenty minutes' duration, without associated symptoms. At the time, this was thought to have been caused by a splenic infarct. Following this the jaundice became prominent, and purpuric spots were seen over the thorax and the abdomen; the patient gradually failed, and died twenty days after admission.

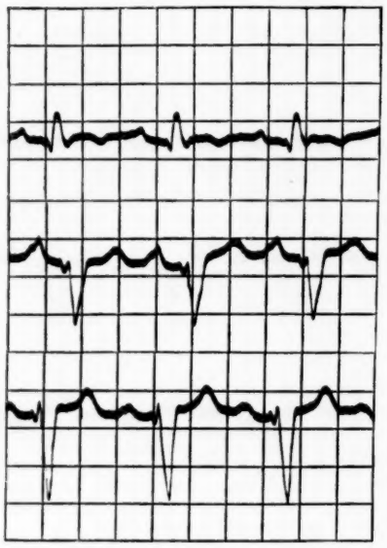

Fig. 5 (case 2).—The tracing reveals the following: a rate of 92; sinus tachycardia; left ventricular preponderance; inverted T wave in lead I; incomplete bundle-branch block (Q-R-S interval, 0.12, 0.14 and 0.14 second), and exaggerated P wave in lead II.

The pericardium measured transversely 20 cm. and contained 100 cc. of bile-stained fluid. The heart weighed 540 Gm. There were patches of epicardial thickening, known as soldier's patches, about 2 cm. in diameter on the anterior surface of both the right and the left ventricles and on the left auricle. The myocardium was reddish brown, and there was streaking of only slight degree. In the left ventricle, near the apex, was a huge infarct which on cut section revealed marked fibrous change. On the endocardial surface of this infarct was a huge, adherent mural thrombus, extending nearly to the base of the aortic valve. Both ventricles and both auricles were dilated moderately, and the wall of the left ventricle was markedly thinned (fig. 6), especially in the region of the infarct. The right coronary artery appeared normal; examination of the left coronary artery, just distal to the orifice, revealed sclerosis to a severe degree, and this continued throughout the distribution of the vessel. Microscopic study of the vessels gave evidence of occlusion due to intimal thickening. There was no evidence of inflammatory reaction.

Fig. 6 (case 2).—Extensive chronic infarction, large intramural clot, and thinned out and sclerotic walls of left ventricle.

The remainder of the examination disclosed anasarca and passive congestion of the visceral organs. There were infarcts in the lungs, spleen and right kidney. The arteriosclerosis of the aorta was only of slight degree. An accessory spleen and healed duodenal ulcer were present.

SUMMARY

Myocardial infarction resulting from coronary thrombosis (primary sclerosis) is relatively rare if patients are less than 40 years of age. The cases reported here and those in the literature prove that it may occur early in the third decade of life. Moreover, there is reason to believe that this condition affected one patient who was 18 years of age and two who were in the twelfth year of age.

It would appear that coronary thrombosis with infarction in young persons is a cause of cardiac enlargement and may produce marked enlargement in a relatively short time.

The enlargement does not appear to be a true hypertrophy in the sense that hypertrophy is taken to mean enlargement of the individual muscle fibers. Whether the infarction produced a metabolic disturbance in the muscle fibers, and this resulted in an increased volume, can only be conjectured.

THALLIUM POISONING

A PRELIMINARY REPORT OF ELEVEN CASES AT THE GENERAL HOSPITAL OF FRESNO COUNTY, CALIFORNIA *

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AND
C. E. NIXON, M.D., PH.D.
FRESNO, CALIF.

The toxic action of thallium was first noted in 1865 by Lamy.[1] Thallium has had its widest use in recent years as a rodent poison. For this purpose it is usually mixed with barley and distributed in animal runways.

The present report deals with eleven cases of poisoning from the use of barley mixed with thallium sulphate. After the barley had been ground, tortillas (a Mexican bread made by mixing flour and water and rolling the dough into thin cakes) were made from the whole grain.

These patients gave a uniform history of onset of symptoms twenty-four hours after partaking of the tortillas. The first symptoms noticed were a tingling sensation and pains in the hands and feet, followed by severe paroxysmal abdominal pains and vomiting. No diarrhea was observed.

Shortly after the first manifestations, weakness of the extremities developed. This weakness did not involve any particular muscle group except that it was more marked peripherally than proximally. Patients were afebrile but with an acceleration of the pulse rate. The blood picture in the first two to five days was normal. The urine showed traces of albumin and hyaline casts. In all cases there was a marked

* From the General Hospital of Fresno County.

1. Lamy, A.: Compt. rend. Acad. d. sc. 57: 442, 1863.

stomatitis. Some exhibited a purplish line at the junction of the teeth and gums. Marked salivation was present in all cases. Bleb formation appeared on the lips; the breath was foul.

Within two to five days after the onset, all patients showed evidence of cerebral involvement manifested by cranial nerve palsies and disturbed sensorium and choreiform or myoclonic movements of the extremities and the head. Among the cranial nerve manifestations, ptosis, strabismus and dilated pupils which reacted feebly to light were prominent. Falling out of the hair occurred in all these patients at this time.

The deep reflexes varied from time to time in the individual patient as well as in the different patients. In no instance were they lost and at times they were exaggerated. No pathologic reflexes were present.

In the more toxic cases convulsions occurred, which were followed by a marked delirium, after which patients became comatose and died of respiratory failure. Within twenty-four to forty-eight hours prior to death there was an elevation of temperature up to 103 F. with pathologic changes in the chest indicative of a bronchopneumonia or pulmonary edema.

Observations in Eleven Cases of Thallium Poisoning

No.	Case	Sex*	Age	Ingested Thallium	Onset of Symptoms	Conditions Observed	Course
1	L. N.	♀	5 years	1/13/32	1/14/32	Pain in extremities and abdomen; vomiting; stomatitis; falling out of hair; convulsions; pulmonary symptoms	Died 1/24/32
2	M. N.	♂	6 years	1/13/32	1/14/32	Pain, tenderness and "numbness" in extremities; abdominal cramps; stomatitis; salivation; vomiting; ptosis; strabismus; myoclonic twitchings; alopecia	Died 1/23/32
3	I. D.	♂	7 years	1/13/32	1/14/32	Alopecia; pains in extremities; thallium in urine.....	Recovered; discharged 2/12/32
4	L. N.	♀	7 years	1/13/32	1/14/32	Pain and "numbness" in extremities; weakness; alopecia; nausea; disturbance of consciousness; choreiform twitchings; convulsions; pulmonary symptoms	Died 1/23/32
5	V. D.	♂	9 years	1/13/32	1/14/32	Pain in extremities and abdomen; falling out of hair; lethargy; ptosis; strabismus; foul mouth; paresis of extremities	Recovered; discharged 2/12/32
6	I. N.	♂	10	1/13/32	1/14/32	Pain in extremities and abdomen; vomiting; weakness; hyperactive reflexes; alopecia; cranial nerve palsies; stomatitis; lethargy; twitchings; coma	Died 1/24/32
7	C. D.	♀	29	1/13/32	1/14/32	Pain and "numbness" in extremities; abdominal cramps; dilated pupils; falling out of hair; coma	Died 1/28/32
8	N. N.	♀	32	1/13/32	1/14/32	Vomiting; epigastric pain; shooting pains and paresthesias in extremities; falling out of hair; ptosis; strabismus; stomatitis; delirious; myoclonic twitchings; coma	Died 1/26/32
9	A. D.	♂	33	1/13/32	1/14/32	Pain in extremities and abdomen; tingling in extremities; hypesthesia in fingers and toes; foul breath; weakness of extremities; salivation; alopecia; myoclonic twitchings; psychosis	Still in hospital; psychosis
10	I. N.	♂	34	1/13/32	1/14/32	Pain in extremities and epigastrium; abdomen tender; salivation; stomatitis; ptosis; hair loose; irrational; optic atrophy	In hospital; shows mental symptoms
11	B. R.	♂	43	1/13/32	1/14/32	Epigastric pains; tingling, tenderness and pains in extremities; hypesthesia; nausea; stomatitis; alopecia; restlessness	Discharged 2/12/32, well except for slight pain and paresthesia in extremities

* In this column, ♂ indicates male; ♀, female.

In the treatment of these patients we used sodium thiosulphate intravenously, 1 Gm. doses twice a day for adults, and 0.5 Gm. doses for children. After this treatment was discontinued because of its apparent failure, sodium iodide was similarly given in 2 Gm. doses. Two of the patients were given calcium lactate and parathyroid extract. In addition to these, dextrose and salt solutions and other symptomatic therapeutic measures were used as indicated.[2]

2. At the present time, five weeks after onset, three patients (two children and one adult) have been discharged from the hospital. Except for the alopecia, all were free from symptoms and the urine was negative for thallium. Two adult male patients still have evidence of peripheral neuritis, show mental changes, and have traces of thallium in the urine.

The Bursting of a Paper Bag.—Noise has an effect upon the brain. Morphine and nitroglycerin are known to raise the blood pressure in the brain more than any other drugs; yet experiment has proved that the bursting of a paper bag raised the blood pressure more than either of these drugs, and four times the normal, for seven seconds, and that it did not return for thirty seconds; in addition, there were increased pulse rate and irregular action of the heart.—Warren, Charles: Effects of Noise on the Nervous System, *M. J. Australia* **1**:49 (Jan. 9) 1932.

RADIUM POISONING *

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WASHINGTON, D. C.

A serious hazard in luminous dial painting has been recognized only since 1924, though fatal cases of poisoning by radioactive material in that occupation had occurred during the two preceding years. Several investigations and studies of the condition were made and have been summarized by Martland.[1] The poisoning has shown itself by bone disease, especially necrosis of the jaw, and by anemia. All the reported cases have occurred in the United States, although the industry is carried on in several European countries. The practice of pointing the brush with the lips, which the girl workers were taught in the United States, probably contributed largely to the incidence of the disease, and this has not occurred since 1926. The use of mesothorium as a constituent of the paint has also been discontinued; mesothorium has a more rapid decay than radium, although giving off more active radiation. The paint itself is prepared by moistening a dry powder, which consists largely of zinc sulphide, with minute amounts of radioactive salts, varying with the grade of the paint through a considerable range. In order to minimize painting by hand, mechanical processes are now used in part, either transferring the paint from a die to the watch face by means of a transfer press or dusting the dry luminous powder on dials previously painted with nonluminous adhesive.

On account of the insidious, prolonged, yet striking course of the disease, the subject of radium poisoning has been given much newspaper publicity. Subsequent to the investigations of luminous dial painting, which had been sponsored by the manufacturers and others, the Surgeon General of the United States Public Health Service held a conference on the subject, Dec. 20, 1928, as a result of which an investigation was undertaken to determine the remaining hazards, if any existed, and means for prevention. It would be

* From the Office of Industrial Hygiene and Sanitation, United States Public Health Service.

* Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 10, 1931.

1. Martland, H. S.: Occupational Poisoning in Manufacture of Luminous Watch Dials, J. A. M. A. **92**: 466-473 (Feb. 9), 552-559 (Feb. 16) 1929.

impracticable to acknowledge here by name all those who have helped in this study. This paper is a brief summary of some of the material covered in a forthcoming report of the investigation, to be published in *Public Health Reports* by Thompson, Schwartz, Makepeace, Ives, Knowles, Britten, Bloomfield and Dean.

The investigation covered all the dial painting factories in the United States with the exception of a few employing only one to three workers. It included an occupational analysis, a determination of the radioactivity of the dust in the workrooms (both dust in the air and settled dust), an electroscopic determination of the amounts of gamma and beta radiation and gaseous radium emanation in various parts of the workroom, of gamma radiation from the bodies of the workers, and tests of the exhaled air for evidence of radium and thorium emanations; the medical examination included blood counts and hemoglobin estimations, and the dental examination included roentgenologic examination of the bones of the jaws. Attention was directed to the workers exposed only since 1926, when the habit of mouth-pointing the brushes was completely abandoned; but, in order that the survey of the present situation should be complete, all those at work were examined, as well as some who had stopped work on radium, and others, serving as controls, who had not been exposed to any possible hazard of this kind. Except in a few cases, workers who had been found by the companies' examinations to be definitely radioactive and who had consequently been removed from work on radium were not examined.

The test group consisted of workers exposed only since 1926; those who had at least part of their experience prior to that year constituted the positive control group, and those without radium exposure the negative control group. In the comparison of the test group with the positive control group there were two important modifying factors. In the first place, exposure of the former, the test group, exposed only since 1926, was for a shorter time than that of the latter, so that less average effect would be expected; on the other hand, the workers who had been severely affected under the old and obviously more dangerous conditions were not examined, and the positive control group therefore gave a more favorable picture of the old conditions than if all the former employees had been subjected to examination. In addition to the regular painting of dials and hands for watches and clocks there are several associated tasks, such as inspecting the completed product, weighing and mixing the paint, and recovering radioactive material from old or rejected dials, all of which were considered in the survey.

The dust collected from the air near the breathing points of the workers was found in some cases to be definitely more radioactive than dust similarly collected from the general air in the workrooms, though the difference was not great for those painting by hand. For some of those using mechanical processes and for some of those at other tasks, the amounts were considerably more. Settled dust on areas above the floor level and in cracks of the floor was also found to be somewhat radioactive, but a cloth which had been used for wiping paint brushes, glass stirring rods, crucibles and table tops was found to contain over ten times as much radium as that judged from samples to be present in all the settled dust in the room, exclusive of that on the floor.

Electroscopic readings were also made at various parts of each workroom for gamma and beta radiation, and samples of the air were taken for gaseous radium emanation. As was to be expected from the character of the work carried on, these were positive and simply show the variations in gamma and beta-ray and radon exposure to which the workers as a whole were subjected from sources outside their own bodies. The actual figures would of course vary greatly from time to time in accordance with the amount of radioactive material exposed on the workbenches. The number of the test group of workers was too small for them to be considered by individual factories. There were differences, however, in the amount of protection given to the workers in different factories, and in general the lower levels of radium dust concentration in the air were associated with better ventilation, less crowding, stricter supervision, the use of small amounts of paint, and the avoidance of handling dry paint.

The individual workers were examined for gamma radiation from their bodies, and in most instances for the gaseous radium or mesothorium emanation in their exhaled breath. In general, the observations as to gamma radiation were confirmed by the observations as to radium emanation or thorium emanation. In the test group comprising those workers employed only since 1926, there was no definite evidence of thorium emanation. In all those examined, including the positive control group, the amounts of radioactivity found, when there was a positive reading at all, were much smaller than those reported for severe and fatal cases of radium poisoning. Electroscopic readings are so delicate and so much influenced by various factors that it seems much safer, especially in these smaller values, to consider a group of individuals as a whole rather than individual cases. This was the method employed in the survey. In the test group the average reading for those employed two years was approximately half a microgram.

Skin examinations, including fingerprints of all workers, to detect slight radium burns, gave entirely negative results. Examination of the blood showed no significant difference between the test group and the negative controls.

In the dental examinations, roentgenograms of the alveolar regions were taken because these regions had most frequently shown bone changes in cases of definite radium poisoning in dial painters, and because these regions offered the best place for roentgenography of bones with a minimum interposition of soft parts. Furthermore, there is a wider basis for comparison with normal variation than in almost any other part of the body, on account of the frequency with which dental roentgenograms are made. In the positive control group of workers with exposure before 1926, these films disclosed two conditions that appeared to be of importance in the study: focal atrophy and focal sclerosis. The sclerosis was distinctly greater than that which could be attributed to an ordinary apical abscess. The atrophy was more important and could not be attributed to any known dental cause. These bone changes, however, were slight compared to the severe lesions which have been described in marked cases of radium poisoning. It was striking that these changes were correlated with the gamma-ray readings of the individuals in which they occurred; each of the four workers having more than 4 micrograms of radium, according to the method of estimation used, showed this condition. With decreasing values of the gamma-ray readings, a smaller percentage showed the bone changes, and there was no definite evidence of change in the test group; that is,

those employed since 1926. The intensity of the condition was also more marked in the cases with gamma-ray readings above 1 microgram than in those with less than 1 microgram. This indicates that even the low gamma-ray readings found in this series are of significance when considered as a group. The determinations of radioactivity in the dust of the working places show that there is present enough active material to account, in part at least, for radioactivity of some of the workers.

It appears that it should be possible for the industry to be conducted with entire safety. Of the possible sources of ingress of radioactive material (ingestion, skin absorption, and inhalation), massive ingestion by pointing the brush in the mouth has apparently been stopped. There is no evidence of skin absorption or of harmful alpha, beta or gamma radioactivity from sources outside the body. The inhalation of radioactive material as dust or as gaseous emanation is more difficult to control and deserves especial emphasis. The amounts of radium found in the workers are small, relative to those which have previously been noted in serious or fatal cases of radium poisoning, but the fact that this is true in the few workers examined does not give assurance of safety if a large number were employed or if the present exposure continues over a longer period. Even more than in other dust hazards, such as those of silica and lead, in which the effects are slow in appearing, the inhalation of radium dust should be kept below the point of equilibrium between intake and elimination, because great harm may be done before the condition becomes clinically noticeable or detectable by methods which at present can be easily applied. Though there is evidence, in this investigation, of accumulation of radioactive material even under the improved conditions which have obtained since 1926, there is no indication that the accumulation since that date has in any individual case been sufficient to injure the worker. The evidence does, however, show the necessity for a still further and marked reduction of the exposure, not only barely to prevent further accumulation, but also to provide a sufficient factor of safety under varying conditions and varying susceptibilities.

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ABSTRACT OF DISCUSSION

DR. EMERY R. HAYHURST, Columbus, Ohio: A case of industrial radium poisoning has never been reported to official agencies in Ohio. Both radium and manganese poisoning were added to the list of compensable occupational diseases by the Ohio legislature two years ago, but no cases of either have been reported as a consequence. I am not convinced that the cytologic changes recently reported by Schlundt, McGavoch and Brown of Missouri in refiners of radioactive substances are not without significance, though they report that no accumulative effects were noted and the radioactivity acquired during employment did not become fixed in the body. These authors consider the principal sources of danger the hard gamma rays from mesothorium 2, radium C and thorium C″, while the dangers from the radioactive gases radon and thoron are either slight or easily controlled; also that 10 micrograms of radium deposited in the body constitutes the tolerance limit of the average person. At the Manchester and District Radium Institute, England, where the blood of the staff workers is regularly examined, the evidence shows, according to Birkett, that even in casual workers there is a slight stimulation of the bone marrow. In the recent symposium of papers on radiology in THE JOURNAL, May 23, 1931, Wood calls attention to possible sensitization produced by radium in patients, and defines the number of roentgen units required to give a skin erythema as about 500, measured in the air; also that any marked diminution in leukocytes or hemoglobin calls for a prolonged holiday—in fact, every one exposed to scattered x-rays or radium should be given four weeks' vacation a year. Pancoast emphasizes that distance is the best protection while handling radium elements, such as long forceps for the protection of the hands and a thick lead shield for the body, while all handlers should have a rotating service; also that the blood picture constitutes the danger signal, while the hands and fingers must be watched for damage to the skin and nails. Finally, Flinn reports a series of cases of radium poisoning, presumably from the New Jersey exposures, which, although showing even the "moth eaten" calvarium and other pathologic changes in the bones (according to roentgen observations) were favorably affected by viosterol. It could be shown that viosterol caused a gradual decrease of radium present in the body and of the pathologic changes in the bones, and an increased rate of elimination of the radium, amounting to 35.5 times what it was before treatment began. From all these recent reports it would appear that radium need no longer be considered a serious industrial hazard since an early index of its body effects and methods of safe manipulation are now known.

DR. HARRISON S. MARTLAND, Newark, N. J.: I have been of the opinion that blood examinations were of little importance in diagnosing radium poisoning unless the radium dial painter had a severe anemia, and that was always toward the end of the disease, so that the point of determining whether dial painters are potential subjects for radium poisoning depends entirely on the determination and quantitative estimation of radium and mesothorium in their bodies during life by means of electroscopic tests. There is no other known method. Concerning prevention, it would seem that regulations should be suggested to the various states covering the occupational and professional dangers and hazards in the handling of radioactive substances. As I understand this report, it shows that dial painters who have never licked brushes and apply the luminous paint by modern means with every precaution taken to prevent harmful effects still become radioactive. The study of a large series of these workers shows an average of 0.5 microgram. Of course, it must be realized that the detection of 0.5 microgram of radioactive substances in the body during life is a difficult thing and only expert physicists are capable of detecting these small amounts, if at all. I am of the opinion that the normal radioactivity of the human body should not be increased in any way because of the possibility of the development of malignancy in radioactive persons. Concerning the possibility of eliminating some of the radium in these cases, I am now willing to change or at least modify my former views. In 1925 I stated that these dial painters had swallowed insoluble sulphates of radium and mesothorium and because of their great insolubility there was no way of eliminating the final deposits in the bones except by their own uninfluenceable natural decay. The only means I knew of was to incinerate the skeleton and extract the radioactive substances chemically. That was before Aub's treatment of lead poisoning was described. Dr. Flinn has recently told me that one can eliminate a considerable amount of radium by following Aub's method of decalcification. In the treatment of lead poisoning by Aub's method, the easy part of the lead to get rid of is that which is last deposited in the trabeculated portions of the bones. It is questionable whether the lead finally deposited in the dense cortex can ever be eliminated. The same statement applies to radium, with this difference, that the lead in the cortex is inert and not dangerous, while radium is constantly irritating because of its uninfluenceable radiations. I will say, therefore, that the treatment advocated by Flinn is the only logical one for radium poisoning at the present time and that it should be given with great persistence in all cases showing appreciable amounts of radioactivity.

FREDERICK B. FLINN, PH.D., New York: I have been associated with the radium industry for six years and am aware of the hazards. I think emphasis must be put on the dust hazard in a working room, as that is an important factor. The trouble is the complacence that has been shown by the manufacturers. They say, "We have had no cases in our plants," and consequently they feel that they have overcome the hazards. There is need for such a survey to bring out the hazard that still remains. I think it is rather to be regretted that the

service has not had a chance to examine industries that existed in 1926 in which all the cases on record became radioactive. Contrary perhaps to Dr. Leake's understanding, many of those showed from 150 to 180 micrograms inside of six, eight, nine or ten months and a year. I think if one will take the average of all the girls who worked in the industry who became radioactive one will find that nearly a year and a half has elapsed. Dr. Martland and I have agreed that 10 micrograms seems to be the tolerance limit. So far we have not found a case which has shown any injury in which 10 micrograms or more was present. I think the limit should be cut down to less than that. The electroscope is the only reliable method for detecting radioactivity or determining whether or not an employee is overexposed. The trouble is that there are only a few people who are qualified to carry it out. What is more important to the medical profession is that it has been thought that the radium hazard was confined to radium workers in the plants. When the radium hazard was first exposed I raised the question why it was that there were no cases of radium poisoning among those treated with intravenous injections of radium chloride. There are some investigations made showing that radium chloride injected into an animal produces exactly the same bone changes that occur in human beings. I have had people who have been treated by physicians intravenously and they have shown the same picture that has been found in the animals. The jaw condition and everything is there. In one case there was 43 micrograms and in another case 33 after some of these radium preparations had been partaken of. I am not referring to radium waters, which contain only the gas and probably are eliminated before they ever reach the stomach or the rest of the body.

A SPECIFIC HEMATOPOIETIC HORMONE IN NORMAL GASTRIC JUICE

PRELIMINARY NOTE *

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GEORGE BURGER, M.D.
AND
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The researches of Castle and his co-workers [1] have thrown important light on the rôle of achylia gastrica in pernicious anemia and represent the most important advance in the study of this disease since the introduction and development of liver therapy by Minot and his associates.

It has been shown by Castle that the gastric juice in pernicious anemia is lacking in some vital factor. He has found that when beef which has been digested by normal gastric juice is fed to the patient ill with pernicious anemia, a reticulocyte response occurs within ten days, comparable to that obtained with liver therapy. If, on the other hand, the beef is digested with the gastric juice from a patient ill with pernicious anemia, its ingestion no longer stimulates an increase in the reticulocytes. The same negative result was obtained when beef predigested by artificial gastric juice was given to patients with pernicious anemia. Next, normal gastric juice was given by mouth to patients with pernicious anemia. While gastric juice plus beef had been found to be effective in causing a reticulocyte response, gastric juice alone was without effect.

Castle and his associates have shown that the essential unknown factor of the gastric juice which is absent in the exacerbation of pernicious anemia is not hydrochloric acid, pepsin or rennin. Furthermore, they have demonstrated that this unknown substance is destroyed by boiling for five minutes, by heating to from 70 to 80 C. for one-half hour or by exposure to a temperature of 40 C. for three days.

It occurred to us (R. S. M.) that the unknown factor, which Castle demonstrated to be absent in the gastric juice of pernicious anemia, might be effective when given intramuscularly or intravenously, though he had shown that it was inert when given by mouth in the amounts contained in 300 cc. of normal gastric juice daily for ten days.

By experiment, first on animals and later on man, we [2] have found that normal gastric juice, after neutralization, may be injected intramuscularly without undue local or general reaction. We have given a few doses intravenously but have abandoned this method for the present, because of the reactions that occurred in some cases.

Gastric juice for our experiments has been obtained from the fasting stomachs of individuals free from anemia. After preliminary lavage, subcutaneous injection of histamine has been given and the resulting secretion collected.

The intramuscular injection of from 10 to 20 cc. of normal gastric juice gives a reticulocyte response so slight as to be negligible. Next, we tried concentrating the gastric juice. This was accomplished, in our earlier experiments in November, December and January, by allowing normal gastric juice to evaporate in an incubator. It required between two and three days to secure a reduction to about one-tenth the original volume. Almost daily intramuscular injections of amounts equivalent to from 100 to 250 cc. of gastric juice have been followed by a reticulocyte response of from 5 to 6 per cent. This treatment, continued for a month, has produced a gradual increase in the red count, white count and hemoglobin, and the platelets in stained films became much more numerous. The response, while definite, has been inferior to that obtained with other preparations. But, owing to our method of concentration, i. e., evaporation in the incubator at 38 C. for from two to three days, we felt that the unknown substance had been partly inactivated, as Castle has shown that normal gastric juice, after exposure for three days to a temperature of 40 C., becomes inert when added to beef. We have therefore resorted to vacuum distillation at a temperature not exceeding 40 C. and have

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1. The work has been described in the following articles:
Castle, W. B., and Locke, E. A.: Observations on the Etiological Relationship of Achylia Gastrica to Pernicious Anemia, J. Clin. Investigation **6**: 2 (Aug.) 1928.
Castle, W. B.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: I. The Effect of the Administration in Patients with Pernicious Anemia of the Contents of the Normal Human Stomach Recovered After the Ingestion of Beef Muscle, Am. J. M. Sc. **178**: 748 (Dec.) 1929.
Castle, W. B., and Townsend, W. C.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: II. The Effect of the Administration to Patients with Pernicious Anemia of Beef Muscle After Incubation with Normal Human Gastric Juice, Am. J. M. Sc. **178**: 764 (Dec.) 1929.
Castle, W. B.; Townsend, W. C., and Heath, C. W.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: III. The Nature of the Reactions Between Normal Human Gastric Juice and Beef Muscle Leading to Clinical Improvement and Increased Blood Formation Similar to the Effect of Liver Feeding, Am. J. M. Sc. **180**: 305 (Sept.) 1930.
Castle, W. B.; Townsend, W. C., and Heath, C. W.: Further Observations on the Etiological Relationship of Achylia Gastrica to Pernicious Anemia, J. Clin. Investigation **9**: 2 (Aug.) 1930; Lancet **1**: 1062 (May 17) 1930.
Castle, W. B.; Heath, C. W., and Strauss, M. B.: Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: IV. A biological Assay of the Gastric Secretion of Patients with Pernicious Anemia Having Free Hydrochloric Acid and That of Patients Without Anemia or With Hypochromic Anemia Having No Free Hydrochloric Acid, and of the Rôle of Intestinal Impermeability to Hematopoietic Substances in Pernicious Anemia, Am. J. M. Sc. **182**: 741 (Dec.) 1931.

2. Morris, R. S.; Schiff, L.; Burger, G., and Sherman, J. E.: Reticulocyte Response in Pernicious Anemia Following Intramuscular Injection of Gastric Juice, Cincinnati J. Med. **13**: 27, 1932.

been able to concentrate large volumes of normal gastric juice in from two to four hours.

Vacuum distillation has yielded a highly potent product. Intramuscular injection of this material has been followed by a remarkable, almost immediate, reticulocyte response. Ten hours after the first injection of a concentrate obtained from 450 cc. of normal gastric juice, the reticulocytes rose from 0.5 per cent to 5 per cent and there was striking polychromatophilia. There was also a rise in the total white cell count with a marked increase in the percentage of neutrophils. At the end of thirty-six hours the reticulocytes amounted to 17.6 per cent. The total red cell count at this time was 2,100,000. There were, therefore, approximately 369,000 reticulocytes per cubic millimeter.

Coincident with the rise in the reticulocytes, we have found a marked increase in the number of red cells containing nuclear particles or Howell-Jolly bodies, which will be reported fully later.

The nature of the active principle in normal gastric juice is unknown. In its failure to give results with oral administration and its demonstrated activity when injected intramuscularly, it resembles, for example, insulin and certain pituitary preparations. That it may normally be secreted internally by the stomach seems quite possible.

Our experiments demonstrate that normal gastric juice contains a substance which, when injected intramuscularly, stimulates the bone marrow to a remarkable degree, and, in the light of Castle's work, we believe that the absence of this substance is the cause of pernicious anemia. What relation it may bear to the cord changes in this disease remains to be seen. Its effect on the bone marrow is manifest within a few hours after injection. It acts more rapidly than agents hitherto employed, and even with our crude preparations the degree of response is comparable to that following liver extract or desiccated hog stomach.

For the hematopoietic hormone which we have demonstrated in normal human gastric juice, we have proposed the name *addisin*, after Thomas Addison, who first described pernicious anemia.

This is in the nature of a preliminary report of our work, which will be published in detail later.

Similar studies with the gastric juice of carnivora, omnivora and herbivora are under way, as well as observations on the effect of addisin in other severe anemias.

The Joy of Living.—As I grow older, I have less and less sympathy with the conscientious efforts merely to extend life in old age. The curtailment of activities, the tender nursing, the humane and assiduous attention of doctors are apt, too frequently, to carry the aged tottering by the danger point, and leave them helpless doddering wrecks of humanity. Having arrived at this stage, it seems beyond their power, or desire, to let go the one thing they possess, that shred of life that ties them uselessly to earth. The philosophy of Stevenson's "Aes Triplex" suits me better. He says, "We do not, properly speaking, love life but living." And again, "Does not life go down with better grace, foaming in full body over a precipice, than miserably straggling to an end in sandy deltas?" It is the duty of the doctor to preserve, not only health and life, but joy of living; and if most of us had to make our choice we would take the latter. Why ward off death if in the attempt we kill living? But these, perhaps, are matters over which we have but slight control. The vigorously minded patient knows the hounds are in pursuit, and keeps up the chase in spite of our earnest protests and our pleadings to seek shelter.—Longcope, W. T.: Methods and Medicine, *Bull. Johns Hopkins Hosp.* **50**:4 (Jan.) 1932.

Clinical Notes, Suggestions and New Instruments

GRAPHIC RECORDING OF SPINAL FLUID PRESSURE WITH THE HYDROPHORAGRAPH *

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The design of the hydrophoragraph (water-wave-recorder), made primarily for recording the function of the human ureter, suggested its application for the registration of spinal fluid pressure and the outflow of spinal fluid in drops. Since, to my knowledge, there has heretofore been no device for recording spinal fluid pressure in ink, it was thought that the hydrophoragraph might be of further value for this purpose.

The instrument is a combined water manometer and recording tambour, mounted on a movable and adjustable stand, and consists essentially of the following parts:

Fig. 1.—The hydrophoragraph adapted for reading and recording of spinal fluid pressure and the outflow of spinal fluid in drops. The tambour lever with the recording pen is seen on the right side and the drop recorder pen on the left side of the chart. The electrical drop recorder switch and cord can be seen immediately beneath the paper weight at the end of the chart. The long rubber tube with Y piece in the upper portion at the left side of the instrument is attached to the bottom of the drop recorder cup and to the trough of the chart shield and is for the purpose of conveying the fluid to a receptacle.

1. A glass manometer with a scale in millimeters or centimeters of water pressure. For increased pressures a long glass manometer may be employed, or medium length glass tubes may be stacked on one another, as in the water manometer already in use.

2. A tambour cup with rubber diaphragm the excursions of which are transmitted to the lever recording system.

3. A lever system with a recording pen at its end and a small perforated rod for the application of counterweights. With high pressures the use of counterweights is necessary so that the tambour lever will write on the chart regardless of the pressure encountered. Since counterweights act on the tambour diaphragm, the transmission of this pressure is registered in the glass manometer. This permits the operator to make ready reductions for this weight.

4. Inflow and outflow arms, with valves at their ends, connected to the tambour cup. The outflow arm has a screw valve the closure of which prevents the escape of fluid, while its regulation permits recording without complete loss of pressure. The inflow arm has a two-way valve, which is handy for opening and closing connection between patient and instrument.

5. A chart and kymograph clock mechanism. The chart moves at the rate of 1 inch per minute. A base line has been ruled on the chart for convenience. Notations can be made on the chart the moment phenomena occur by writing against the metal shelf over which the paper passes. The paper roll is sufficiently large for numerous records before replacement is necessary.

6. An electrical drop recorder, for the registration of spinal fluid in drops. This is operated by plugging the cord connection into a 110 volt alternating or direct current circuit, then opening the outflow valve, permitting the drops to pass between electrodes located beneath this valve. The drops are recorded in ink at the top of the chart.

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7. A short piece of thick walled rubber tubing of small bore is used to establish the connection between the lumbar puncture needle and the instrument. One end of the rubber tubing is slipped on to the inflow valve projection, while the other end is armed with an adaptor to fit the lumbar puncture needle (fig. 1).

PREPARATION OF THE INSTRUMENT FOR USE

Preparing the instrument for use consists in sterilization of the interior of the recording unit and rubber tube connection, application of the sterile rubber diaphragm to the tambour cup and of the rubber tube connection to the inflow valve, the filling of the system with sterile physiologic solution of sodium chloride, expelling all air, the closure of both valves and adapter end of the rubber tube connection to prevent loss of fluid from the system, the filling of recording pens with ink, and finally the adjustment of the tambour lever so that its pen writes freely.

The tambour cup with attached arms is made of metal and may be sterilized in boiling water or by immersion in alcohol. The glass manometers may be sterilized by immersion in alcohol or other antiseptic solutions. The rubber diaphragm may be placed in boiling water for a minute or in an antiseptic solution which will not affect rubber. If antiseptic solutions are used for sterilization, it is obvious that the interior of the instrument should be thoroughly washed free of the solution by sterile water or saline solution. The rubber diaphragm and tambour cup must be thoroughly dry before easy and proper application of the diaphragm can be made. Diaphragm application is made with aseptic precautions.

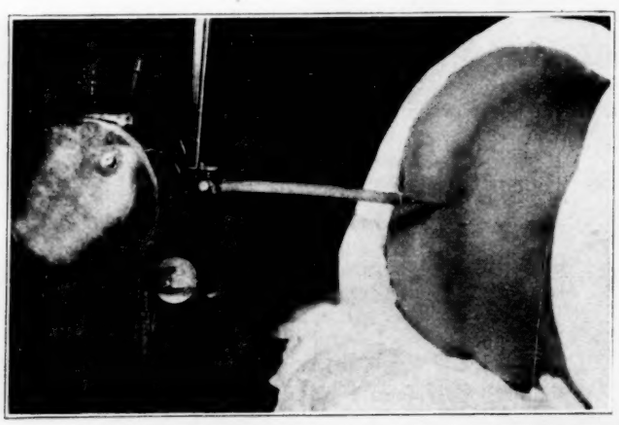

Fig. 3.—The patient is lying on his side. The instrument is connected to the lumbar puncture needle through a short piece of thick walled rubber tubing. The other end of this rubber tube is connected to the inflow valve projection as depicted. Beneath the metal shield with the trough can be seen the paper chart roll. The round drum contains the kymograph clock.

TECHNIC OF USE

The recording unit is raised to the level of the spine with the patient lying on his side. After insertion of the lumbar puncture needle into the subarachnoid space and the obtaining of a flow of spinal fluid, the cap is removed from the rubber tube adapter and the connection between the latter and the needle quickly made. The inflow valve of the instrument is now opened wide. The outflow valve is kept closed, unless the operator wishes to record the spinal fluid in drops, reduce the pressure in the instrument, or the like. Pressure readings are taken by observation of the fluid level in the glass manometer and notation of them made on the chart as indicated in the graphic record (fig. 3).

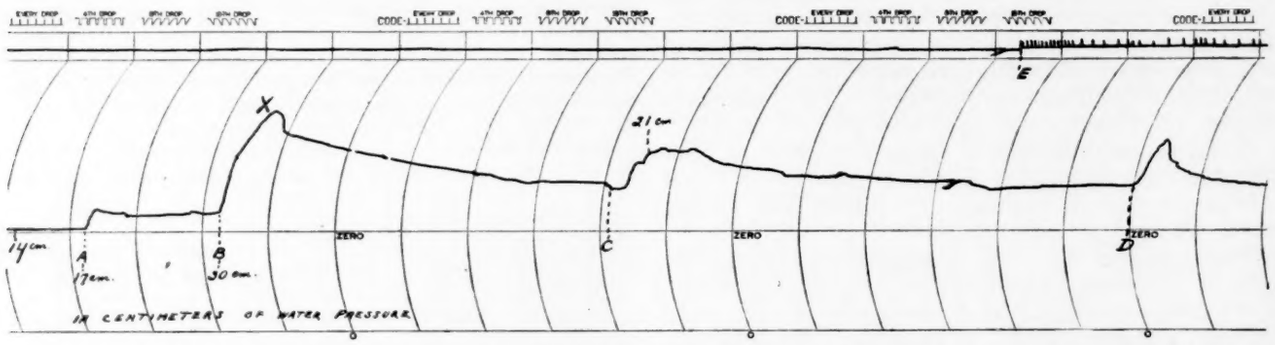

Fig. 2.—The chart and record of spinal fluid pressure. The chart is ruled in minutes and has a base line for convenience. The ruled space at the top of the chart is the drop record. At *A* the pressure rose from 14 cm. to 17 cm., as the result of coughing. *B* marks the point of application of bilateral digital compression to the large vessels of the neck, there being a rise from 17 cm. to 30 cm. The patient was given a hypodermic injection at *C*, the rise in pressure evidently being due to the insertion of the needle. At *D* the neck vessels were again compressed. At *E* the outflow valve was opened and adjusted so that the drops of spinal fluid could also be recorded. At *X* a counterweight was applied to the lever system to keep the pen writing on the chart.

The ink recording lever responds almost as quickly as does the fluid level in the glass manometer to increases or decreases in pressure. The amount of ascent or descent of the lever is obtained from the glass manometer readings (fig. 2).

CONCLUSION

1. The hydrophoragraph has been found to be well adapted for the recording in ink of spinal fluid pressure and the spinal fluid in drops.

2. Laboratory as well as clinical studies may be made of spinal fluid pressure without the inconvenience of smoked paper and interruption of the record, and the like.

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Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY OF THE AMERICAN MEDICAL ASSOCIATION HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE.

H. A. CARTER, Secretary.

ULTRAVIOLET RADIATION USEFUL FOR THERAPEUTIC PURPOSES

SPECIFICATION OF MINIMUM INTENSITY, OR RADIANT FLUX

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During the past few years, experimental data have become available showing that the spectral band of ultraviolet radiation of wavelengths shorter than about 315 millimicrons, in sunlight and in some artificial sources of radiation, if sufficiently intense and if the time of exposure is sufficiently prolonged, has the power of preventing and of curing rickets. This is the underlying basis for exploiting ultraviolet of these wavelengths for general healing purposes. While this point of view may be too broad, the beneficial effects of short wavelength ultraviolet radiation in surgical tuberculosis and certain skin diseases is recognized.

The question at issue is the minimum ultraviolet radiant flux (radiant power) that the source must emit

in order to insure effective therapeutic action. Manifestly, the amount of ultraviolet radiation that can be applied to the body without producing a burn depends on the tolerance of the skin. This can be measured by the erythema produced. It is common knowledge that the erythemal sensibility of the untanned skin is widely different for different persons and also widely different for the same person, depending on the amount of moisture on the skin. Hence the erythemic response is commonly used as an indicator of skin tolerance and of the amount of ultraviolet radiation that can be applied at any one time. Since pigmentation commonly follows a strong erythemic reaction (and even occurs after prolonged suberythemal exposures), it is customary not to continue the exposure longer than necessary to produce a mild or "minimum perceptible erythema"; i. e., one that disappears in the course of twenty-four hours.

In the literature, statements occur that the production of an erythema is unnecessary; that a suberythemal dose is sufficient for the maintenance of health. However, without physical or photochemical measurements, the erythema test is the only means of determining whether appreciable ultraviolet is emitted by the source. Hence, while such statements may be made in good faith, they open the way to fraud by irresponsible venders of alleged sources of ultraviolet radiation. Hence there is need of a specification of ultraviolet intensity. In this connection it is of interest to note that the spectral erythemic reaction is produced only by ultraviolet rays of wavelengths shorter than about 315 millimicrons, with a maximum reaction at the wavelength 297 millimicrons (2,967 angstrom units) and a lesser maximum (55 per cent) in the region of 250 millimicrons.[1] It is to be noted also that in a very general way the spectral erythemic response coincides with the photochemical reaction in the activation of ergosterol (which has the property of curing rickets) and in the curing of rickets by ultraviolet irradiation. However, in the present inquiry this fact is to be considered merely a coincidence that is useful in the evaluation of the output of different sources of ultraviolet radiation and in the specification of the minimum ultraviolet flux (in microwatts per square centimeter) necessary to insure effective results in ultraviolet radiation therapy, as for example in the healing of rickets.

By effective results is meant effecting a cure as quickly and as cheaply as by medicaments. This includes the expense of electric power, heating of the room, service of an attendant, and any factors that may subject the child to other ills (common colds in home treatments) than the one for which ultraviolet is being administered. On this basis, the specification of a minimum ultraviolet radiant flux, of wavelengths less than and including 313 millimicrons, is arrived at from a consideration of the following experimental data and general survey of the question:

1. The observations that my associates and I have made that the untanned moist skin in summer requires an exposure of only about one-half to two thirds as long as in winter (skin dry) in order to produce a minimum perceptible erythema; also, the observations[2] that the midday midlatitude, sea level ultraviolet in summer sunlight, having an intensity of from 80 to 90 microwatts per square centimeter, produced a minimum perceptible erythema in from twenty to forty-five minutes, depending on the person exposed. This is in conformity with the observations of Luckiesh,[3] who records exposures of twenty minutes to obtain a minimum perceptible erythema in midsummer. In winter, on the clearest days at the noon hour, the ultraviolet intensity at sea level (Washington) is only about one-fourth the summer value (20 microwatts per square centimeter), the spectral erythemogenic efficiency is lower, and, with a lower humidity and a drier skin, the time of exposure would be prolonged for from three to five hours, or perhaps longer, to obtain a minimum perceptible erythema.

2. The observations of heliotherapists who obtain the best results by exposing their patients in the forenoon or afternoon in summer, and at the noon hour in winter. The dosage intensity of this (forenoon) "clinical sunlight,"[4] on the present basis of evaluation,[5] is about 30 microwatts per square centimeter, permitting an exposure of several hours without producing an erythema.

3. The observations of numerous investigators[6] who have found that, in order to obtain effective healing of rickets, especially in children (as distinguished from rats and chicks), the solarium windows must have a high transparency to short wavelength ultraviolet radiation. Even under these conditions the exposures were made for several hours each day and had to be continued for two months, or more, in order to effect healing. Assuming that the ultraviolet intensity of winter sunlight was about 25 microwatts per square centimeter and that the window glass transmitted 40 per cent, then the ultraviolet incident on the subjects was 10 microwatts per square centimeter.

4. The experiments of Gerstenberger and Horesh[7] on human infants, partly dressed, leaving the head, neck and the greater part of the extremities free for exposure. These infants were exposed alternately, front and back, in one hour intervals, for twelve hours daily, to an average illumination intensity of 75 foot candles of tungsten filament radiation, produced by a 500-watt Mazda CX lamp, in an aluminum reflector, situated at a distance of 5½ feet above the level of the bed. The healing of rickets began in from one and one-half to two weeks after starting the irradiation, and complete healing was obtained in from nine to eleven and one-half weeks. The three rachitic infants studied received a total of 75,000, 85,000 and 95,000 foot candle hours, respectively.

The point of chief interest in their research, pertinent to the present inquiry, is that, while the dosage intensity was distinctly suberythemal (and at no time was an erythema perceptible, though pigmentation slowly developed), the radiant flux of erythemogenic ultraviolet rays was a little less than 1 microwatt per square

1. Coblentz, W. W.; Stair, R., and Hogue, J. M.: The Spectral Erythemic Reaction of the Human Skin to Ultraviolet Radiation, Proc. Nat. Acad. Sc. **17**: 401, 1931; Bur. Stds. J. Research **8**, March-April, 1932. Gives bibliography of other observers.

2. Coblentz, W. W.; Stair, R., and Hogue, J. M.: A Balanced Thermocouple and Filter Method of Ultraviolet Radiometry, with Practical Applications, Bur. Stds. J. Research **7**: 723, 1931 (research paper 370, obtainable only from the superintendent of documents, 10 cents).

3. Luckiesh, M.: Erythemal Basis for Dual-Purpose Lighting, Tr. Illum. Engin. Soc. **26**: 703 (Sept.) 1931.

4. Greider and Downs: Tr. Illum. Engin. Soc. **25**: 378, 1930.

5. Coblentz, Stair and Hogue (footnote 2); Measurements of Extreme Ultraviolet Solar Radiation by a Filter Method, Bur. Stds. J. Research **6**: 951, 1931 (research paper 318, superintendent of documents, 10 cents).

6. Tisdall, F. F., and Brown, Alan: Antirachitic Value of the Sun's Rays Through Various Special Window Glasses, Am. J. Dis. Child. **34**: 742 (Nov.) 1927. Wyman, E. T.: Boston M. & S. J. **197**: 376 (Sept. 8) 1927. Caldwell, G. W., and Dennett, R. H.: The Clinical Value of Sunlight Through Ultraviolet Transmitting Glass, J. A. M. A. **92**: 2088 (June 22) 1929. Wyman, E. T.; Drinker, Philip; and MacKenzie, K. H.: Antirachitic Value of Winter Sunlight in the Latitude of 42° 21′ (Boston), Am. J. Dis. Child. **39**: 969 (May) 1930. Fleming, W. D.: Mil. Surgeon **62**: 592 (May) 1928.

7. Gerstenberger, H. J., and Horesh, A. J.: The Cure of Infantile Rickets with Tungsten-Filament Radiation, J. A. M. A. **97**: 766 (Sept. 12) 1931.

centimeter. While this seems to be a successful demonstration that erythemogenic ultraviolet radiation of low intensity is effective in healing rickets, it appears that medicaments or a higher intensity of ultraviolet radiation would have been quicker in action. For example, a fourth infant, with moderately severe rickets, who was exposed, front and back, at a distance of 80 cm. (30 inches) for one and one-half hours daily, to an intensity of illumination of 1,200 foot candles of Mazda CX tungsten filament radiation, was completely healed of rickets within seven and one-half weeks. In this case, according to their published data, the intensity or flux of ultraviolet erythemogenic radiation to which the infant was exposed was about 10 or 11 microwatts per square centimeter. They comment on the fact that the rickets healed rapidly and that the blood serum calcium and phosphorus reached normal levels five weeks after the exposures were begun. As a matter of record, it is relevant to add that at this short distance the heat of the lamp caused profuse sweating and that definite pigmentation was noted after three weeks of exposures.

Excessive heating of the patient may be an objectionable feature in general body irradiation, which can be avoided by using a source that emits a high intensity of short wavelength ultraviolet radiation relative to the total emitted by the lamp and the reflector. This will permit operating the lamp at a sufficient distance from the patient and yet obtain an effective dose of ultraviolet radiation.

Owing to the long time required in making the exposures, it appears that lamps of low ultraviolet intensity will prove impracticable for therapeutic purposes, as differing from their possible application for so-called health maintenance, in dual purpose lighting, with which question the present specification is not concerned.

The possibility of shortening the time of exposure is illustrated in the earlier researches of Gerstenberger and his collaborators,[8] in which it was found that curative results were obtained by exposing the infants, front and back, once a week, to an erythemal dose of ultraviolet radiation produced by either a quartz mercury vapor lamp or an early model of the Mazda S-1 lamp, which is essentially a mercury vapor arc between the upper part of a V-shaped helical tungsten filament lamp. In this case the intensity of the erythemogenic ultraviolet radiation, of wavelengths less than and including 313 millimicrons, at a distance of 30 inches from the lamp, in its reflector, was of the order of 110 microwatts per square centimeter,[9] producing a definite erythema in eleven minutes.

In connection with the foregoing citation, it is of interest to include a reference to some short exposure experiments by Maughan and Dye[10] on the amount of ultraviolet necessary to cure rickets in chicks, in which they used a 110 volt quartz mercury (Uviarc) lamp. The ultraviolet intensity is not given, but it is known to be relatively high. In some cases the exposures were made for one and one-third minutes daily. In other cases, four exposures a week, each exposure continuing for less than ten minutes, caused as satisfactory a recovery as the same total exposure (thirty-seven and a third minutes) given in twenty-eight doses of one and one-third minutes each.

5. The admitted fact that the influence of radiant energy on the health of healthy persons is not established.[3] When one considers that animals and human beings have subsisted for years underground, in coal mines, in dark inclosures, and under dark clothing that covers practically the whole body, the present solicitous attention to the amount of ultraviolet necessary for the maintenance of health seems to be overdone. Nevertheless, the problem is here and should be given intelligent, unbiased consideration.

It is not my intention in the present specification to include the ultraviolet requirements of dual purpose lighting for the maintenance of health. In the absence of observational data, the dual purpose requirement is admittedly a conjecture. From the data pertaining to rickets, Luckiesh[3] estimates that a daily exposure to an intensity of from one third to one tenth of a curative dose should be sufficient as a preventive. Nevertheless, while this value may perhaps be sufficient to maintain health,[11] in a recent discussion of the problem[12] it was shown that it would be good practice to use 25 per cent of the minimum perceptible erythemal dose as a basis in planning ultraviolet ray installations for daily use. This is equivalent to about 25 microwatts per square centimeter of the short wavelength ultraviolet in midsummer midday sunlight.

From the foregoing survey it appears that even in the proposed dual purpose lighting, for health maintenance, the radiant flux is not much different from that used in heliotherapy, involving long exposures to sunlight.

6. The observations[13] on the total amount of energy required to excite a minimum perceptible erythema, produced by the standard line of maximum erythemogenic power at 297 millimicrons (2,967 angstroms). These values range from 452,000 to 645,000 ergs per square centimeter, averaging about 500,000 ergs per square centimeter in the winter when the humidity is low and the skin is dry.

In the summer time (high humidity, skin moist) the total energy required to produce a minimum perceptible erythema on the same subjects[2] ranged from 189,000 to 474,000 ergs per square centimeter, averaging 200,000 ergs per square centimeter. In the latter tests, the radiant flux (intensity) was 316 microwatts per square centimeter, requiring an exposure of from one to two minutes to produce a minimum perceptible erythema.

Assuming that in the previously cited short exposure tests by Gerstenberger[8] the intensities were about 110 microwatts per square centimeter (the time of exposure was eleven minutes, the total energy required to produce an erythema was 726,000 ergs. Since the erythemogenic efficiency of the source (Mazda S-1 Sun lamp) is about 24.8 per cent that of the standard 2,937 angstrom line, the 726,000 ergs of heterogeneous ultraviolet radiation are equivalent to about 182,000 ergs of radiation of maximum erythemogenic effectiveness, which is in accord with our exposure tests[2] on untanned adults.

8. Gerstenberger, H. J., and Hartman, J. I.: Quartz Lamp Therapy in Human Rickets and Rachitic Spasmophilia, J. A. M. A. **92**: 367 (Feb. 2) 1929. Gerstenberger, H. J., and Russell, G. R.: Sunlight Type S-1 Lamp (G. E.) Therapy in Human Rickets and Rachitic Spasmophilia, ibid. **94**: 1049 (April 5) 1930.

9. Forsythe, W. E.; Barnes, B. T., and Easley, M. E.: J. Optic. Soc. America **21**: 30 (Jan.) 1931.

10. Maughan, G. H., and Dye, J. A.: The Amount of Ultraviolet Radiation Necessary to Cure Rickets, J. Optic. Soc. America **20**: 279 (May) 1930.

11. Just as though ultraviolet radiation were a preventive for every ill to which man and beast are heir, rather than for a very limited number of ailments.

12. Porter, L. C.; Egeler, C. E., and Sturrock, W.: Ultraviolet Lamps and Equipment, and Their Application for the Maintenance of Health, read before the Illuminating Engineers Society, Pittsburgh, Oct. 13, 1931; Tr. Illum. Engin. Soc. **27**: 23 (Jan.) 1932.

13. Coblentz, Stair and Hogue (footnote 1). Luckiesh, M.; Holladay, L. L., and Taylor, A. H.: Reaction of Untanned Skin to Ultraviolet Radiation, J. Optic. Soc. America **20**: 423 (Aug.) 1930.

SPECIFICATION OF MINIMUM INTENSITY

Since the ultraviolet radiation emitted by various sources differs so greatly in spectral quality and, hence, in erythemogenic effectiveness, the logical specification of the dosage of ultraviolet radiation, of wavelengths useful for therapeutic purposes, is in terms of a homogeneous wavelength having a maximum erythemogenic action. This wavelength is at or close to the emission line of mercury, at 2,967 angstroms (297 millimicrons), which line has a high intensity and is easily obtainable as a standard source for biologic (erythemal) tests.

Using the emission line at 2,967 angstroms as a standard, the radiant flux and the time (which gives the total energy utilized) for producing a minimum perceptible erythema have been determined.[2] Furthermore, the erythemogenic effectiveness of various sources (the sun, the Mazda S-1 lamp, and the like) relative to that of the standard emission line, at 2,967 angstroms, has also been determined by radiometric and erythema tests.[2] These tests are in good agreement, giving an erythemogenic efficiency of 22 per cent for sunlight, 24.8 per cent for the Mazda S-1 lamp, 42 per cent for the blue flame carbon arc lamp, and about 16 per cent for the Mazda CX tungsten filament radiation.

Turning now to the survey of the data summarized in captions 1, 2, 3, 4, 5 and 6, it will be noticed that in the sunlight tests, in which the patients can be placed outdoors for several hours a day, the ultraviolet intensities range from 20 to 30 microwatts per square centimeter. For health maintenance [12] the radiant flux is placed at 25 per cent of the value required to produce a minimum perceptible erythema, or about 22 microwatts per square centimeter of the ultraviolet in summer sunlight, when average sunlight (90 microwatts per square centimeter) requires exposures of twenty minutes or more to produce a slight erythema.

It is to be noted that all these suberythemal intensities, which are equivalent to about 5 microwatts per square centimeter of radiant flux of the standard emission line at 2,937 angstroms, require long exposures, amounting to several hours or longer to effect results.

The short exposures (eleven minutes, once a week, cited under caption 4) which gave effective healing were made with an ultraviolet radiant flux of about 110 microwatts per square centimeter of Mazda S-1 lamp radiation, equivalent to (110×0.248) 27 microwatts per square centimeter of homogeneous radiation of the standard emission line of wavelength 2,967 angstroms.

The most accurate data available [2] were obtained with a radiant flux of about 315 microwatts per square centimeter of the standard emission line at 2,967 angstroms, which produced an erythema, on a moist skin, in from one to two minutes.

If fifteen minutes is adopted as the approximate time of exposure (or a total of thirty minutes for front and back) to produce a minimum perceptible erythema on the untanned skin, it would require a radiant flux of about 20 microwatts per square centimeter of the standard wavelength (2,967 angstroms) radiation. Even with this intensity an erythema would not be produced on the average skin in fifteen minutes, especially after pigmentation has begun. If the time of exposure is shortened to ten minutes, the intensity would be 30 microwatts per square centimeter of wave length 2,967 angstroms radiation.

From a study of the data available, it appears that a comfortable operating distance is from 2½ to 3 feet, depending on the source; that, for effective therapeutic results, it is desirable to expose a large area of the nude body (front and back); and that, from a practicable standpoint, the time of a single exposure, of any portion of the body, should not be continued much longer than fifteen minutes.

Specification.—On this basis the intensity (radiant flux) from sources of heterogeneous ultraviolet radiation, of wavelengths less than and including 313 millimicrons, evaluated according to the spectral erythemic response curve should not be less than the equivalent of 20 microwatts (200 ergs) per square centimeter of homogeneous radiation of the wavelength of maximum erythemogenic effectiveness, which wavelength for practical purposes is taken at the emission line of mercury vapor, 2,967 angstroms (297 millimicrons).

For the various sources of heterogeneous ultraviolet radiation, of wavelengths less than and including 313 millimicrons (3,130 angstroms), the equivalent of 20 microwatts per square centimeter of homogeneous radiation of wavelength 2,967 angstroms, in microwatts per square centimeter, is approximately as follows: the sun, 90; Mazda S-1 lamp, 80; Mazda, S-2, 93; quartz mercury arc, from 60 to 70; "cold quartz," low pressure mercury vapor, 40; carbon arcs, from 50 to 90 (the latter value is estimated, depending on the amperage, the kind of carbons and the presence or absence of a glass window); and the Mazda CX, tungsten filament lamp, 125.

It is to be noted that at the specified operating distance of from 2½ to 3 feet (75 to 90 cm., approximately) the ultraviolet radiant flux from these various artificial sources equals, or even exceeds, the specified minimum values, in all cases excepting the 500 watt Mazda CX lamp. According to Porter and his collaborators [12] a type S-1 lamp (in a reflector) has fourteen times as much ultraviolet output as a 500-watt Mazda CX lamp (in a reflector); that is to say, the intensity of the latter is less than 8 microwatts per square centimeter.[9] This is equivalent to less than 1.5 microwatts per square centimeter without a reflector. My own measurements, 2 feet below the bulb (no reflector) gave a value of 0.75 microwatts per square centimeter. By means of a photo-electric cell, the intensity of the ultraviolet, of wavelengths less than and including 313 millimicrons, at 2 feet below the bulb of a 500-watt Mazda CX lamp (no reflector), was found to be equivalent to the ultraviolet contained in about 50 foot candles of winter sky-light, shining through an open south window, or about one two-hundredth of the short wavelength ultraviolet in midday June sunlight.

Owing to the great amount of heat emitted by this large unit, it would be uncomfortably warm to make the exposures at the short distance that would be necessary in order to obtain a high intensity.[8] The flux of ultraviolet radiation from the 100, 200 and 300 watt units would be still lower than from the 500 watt lamp. For instance, at a distance of 2 feet from a 200 watt "Ultra Violet Sun Bath Lamp" [14] (no reflector) the ultraviolet output was found to be about one thousandth (0.14 microwatts per square centimeter) of noonday sunlight.

In a recent test of Cosmos Sunlike Lamps (no reflectors) the flux (intensity) of ultraviolet radiation, of wavelengths less than and including 313 millimicrons, at a distance of 2 feet (61 cm.) below the bulb of 75, 300, 500 and 1,000 watt lamps was, respectively,

14. Coblentz, W. W.: Sources of Radiation and Their Physical Characteristics, J. A. M. A. **95**: 411 (Aug. 9) 1930.

0.04, 0.24, 0.34 (Mazda CX, 0.75) and 1.05 microwatts per square centimeter.

Hence, while the tungsten filament lamp, in a special bulb that transmits short wavelength ultraviolet radiation, may prove useful in dual purpose lighting and in poultry raising, where all-day exposures can be made, they do not appear to be a suitable source of ultraviolet radiation for therapeutic purposes.

In conclusion it is to be emphasized that this specification of 20 microwatts per square centimeter per second of homogeneous radiation of wavelength 2,967 angstroms, or its equivalent for heterogeneous radiation, is the radiant power that is to be applied. The length of time of each exposure, the number of exposures per week and the total number of exposures (the total energy) required to effect a cure will depend on the person receiving the treatment.

THE UNIT OF DOSAGE

The foregoing discussion leads to the question of what should be the value of the unit of dosage. As indicated elsewhere,[15] the numerical value should be some convenient number, neither too large nor too small.

If a radiant flux of 10 microwatts (100 ergs) per square centimeter per second of homogeneous radiation of the wavelength 2,967 angstroms is adopted and called the Finsen unit (F. U.), then, according to the foregoing specifications, a therapeutic dose of the foregoing sources would be as follows: radiation of the standard wavelength 2,967 angstroms, 2 Finsen units; the sun, 9 Finsen units; the Mazda S-1 lamp, 8 Finsen units; the Mazda S-2 lamp, 9.3 Finsen units; the quartz mercury arc, from 6 to 7 Finsen units; "cold quartz," 4 Finsen units; and the carbon arc lamp, from 5 to 9 Finsen units, depending on the kind of carbon and whether the arc is bare or is shining through a glass window.

The manner of applying this information is interesting. Suppose the sun is used as a source. Evidently the intensity cannot be increased by decreasing the distance. Hence it will be necessary to increase the time of exposure. For example, if the ultraviolet intensity (radiant flux) is only 4.5 Finsen units (45 microwatts per square centimeter) the exposure must be continued twice as long as when the intensity amounts to 9 Finsen units.

On the other hand, if an artificial source of high intensity is being used, for example, a high intensity quartz mercury arc lamp having an ultraviolet radiant flux of 120 microwatts per square centimeter (12 Finsen units) at the standard distance, it would then be necessary to increase the distance sufficiently to reduce the intensity to the standard value (6 Finsen units) or to reduce the time of exposure to one-half the standard value.

From the foregoing, it will be evident why most of the published data now available are inconsistent and misleading. These data do not include a factor that equates the physiologic (erythemal) response. As mentioned before,[2] when this factor is taken into consideration there is good agreement between the observed and the computed time of exposure to produce a minimum perceptible erythema, using sources differing widely in spectral quality and in total intensity of ultraviolet radiation, useful for therapeutic purposes.

2737 Macomb Street, N.W.

15. Coblentz, W. W.: Instruments for Measuring Ultraviolet Radiation, and the Unit of Dosage in Ultraviolet Therapy, M. J. & Rec. **130**: 691 (Dec. 18) 1929.

Committee on Foods

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

HYGEIA PURE STRAINED TOMATOES

Contains Vitamin D

Added Irradiated Ergosterol

Manufacturer.—Snider Packing Corporation, Rochester, N. Y.

Distributor.—Hygeia Nursing Bottle Company, Buffalo, N. Y.

Description.—Strained tomato juice free from seeds, skins and cores retaining in large measure the mineral and vitamin content of the raw tomatoes used; with added vitamin D (irradiated ergosterol), 60 D units per fluidounce; packed in jars. The D units are those defined by the Council on Pharmacy and Chemistry of the American Medical Association (New and Nonofficial Remedies, 1931, p. 414). One fluidounce is equivalent in vitamin D to the D content of one teaspoonful of cod liver oil. No sugar or seasoning is added.

Manufacture.—The tomatoes are purchased on government grades, are thoroughly washed, sorted, scalded and then passed through a cyclone which separates the juice from the seeds, skins and cores. Steam is injected into the cyclone machine to displace the air. The "juice" is concentrated to a specific gravity of 1.05 and again puréed to remove coarse fiber. The latter machine is similar to the first puréeing device but is equipped with a finer screen. The final heated concentrated "juice" is filled into No. 10 cans and processed for a very short period at 100 C. When the product is repacked in the small glass containers it is simply reheated in the original container, run into the washed heated bottles, which are sealed under "vacuum," processed for a few minutes at 100 C., and then promptly cooled.

It is possible that some loss of vitamin C occurs in the concentration of the tomato juice in the open tanks. This loss is minimized, however, by avoidance of inclusion of air during the puréeing process.

Irradiated ergosterol is incorporated in the product as described for the Strained Peas (THE JOURNAL, Feb. 13, 1932, p. 555).

Analysis (submitted by manufacturer).—

Specific gravity 20 C./20 C	1.05
	per cent
Moisture	88.8
Total solids	11.2
Ash	0.7
Fat (ether extract)	0.2
Protein (N × 6.25)	1.5
Reducing sugars as invert	6.8
Crude fiber	0.4
Carbohydrates other than crude fiber (by difference)	8.4
Starch (acid hydrolysis method)	0.3
Calcium (Ca)	0.01
Iron (Fe)	0.003
Phosphorus (P)	0.01

Calories.—0.4 per gram; 11 per ounce.

Vitamins and Claims of Manufacturer.—See these sections for Strained Peas.

BERDAN'S KEW BEE BREAD

Manufacturer.—Berdan Bread Company, Bay City, Mich.

Description.—A white bread made by the sponge dough method.

Manufacture.—The sponge dough ingredients, patent flour, water, yeast and a yeast food containing ammonium chloride, calcium sulphate, sodium chloride and potassium persulphate, are mixed in a high speed mixer. The sponge dough is fermented for from four to five hours, after which are added flour, water, salt, lard, sweetened condensed skim milk and a partially hydrolyzed starch to make the completed dough, which is cut into pieces of desired weight. The pieces are fermented for a short time, molded into loaf form, panned, further fermented,

baked for from thirty to thirty-five minutes, cooled, and wrapped in wax-paper.

The factory, equipment and storage rooms are kept in strictly sanitary condition.

Analysis (submitted by manufacturer).—

	per cent
Moisture (entire loaf)	35.9
Ash	1.8
Fat	2.8
Protein (N × 6.25)	9.0
Crude fiber	0.4
Carbohydrates other than crude fiber (by difference)	50.1

Calories.—2.6 per gram; 74 per ounce.

Claims of Manufacturer.—A bread of good quality.

"GOLDEN" CORN SYRUP WITH CANE FLAVOR

(85 per cent Corn Syrup, 15 per cent Refiners' Syrup)

Packer.—D. B. Scully Syrup Company, Chicago.

Distributors.—Durand, McNeill, Horner Company, Chicago.

Description.—A table syrup; a corn syrup base (85 per cent) with refiners' syrup (15 per cent).

Manufacture, Analysis, Calories and Claims of Manufacturer.—See these sections for Banner Blue Golden Syrup with Cane Flavor (THE JOURNAL, March 5, 1932, p. 817).

GENERAL COMMITTEE DECISIONS

THE COMMITTEE ON FOODS AUTHORIZES THE PUBLICATION OF THE OLLOWING GENERAL COMMITTEE DECISIONS ADOPTED FOR ITS OWN UIDANCE AND THAT OF FOOD MANUFACTURERS AND ADVERTISING GENCIES ON FOOD ADVERTISING. RAYMOND HERTWIG, Secretary.

CHOCOLATE AND COCOA PRODUCTS: SPECIAL RECOMMENDATIONS FOR CHILDREN

Special recommendations for children are not permissible for oods consisting largely of chocolate or cocoa which contain onsiderable quantities of theobromine and caffeine; no objection will be taken, however, to such recommendations in the ase of foods that are merely flavored with chocolate or cocoa nd which, in quantities likely to be consumed, are free from ny probable effects due to theobromine or caffeine, provided he recommendations are permissible for the basic foods hemselves.

DECLARATION OF ADDED SALT OR SUGAR IN SIEVED VEGETABLES OR FRUITS INTENDED FOR INFANT OR INVALID FEEDING OR FOR SPECIAL DIETS

Added salt or sugar in sieved vegetables or fruits intended for infant or invalid feeding or for special diets shall be given appropriate and prominent declaration. This information may be of importance to physicians prescribing their use.

GELATIN NOT AN AID TO THE DIGESTIBILITY OF MILK AND MILK PRODUCTS

There is no satisfactory evidence that gelatin increases the digestibility of milk or milk products. Such claims are not permissible.

"HEALTH FOOD" CLAIMS

The term "health food" and equivalent claims or statements to the effect that a food gives or assures "health" are vague, meaningless and misleading and are not permissible in food advertising. Statements of well established nutritional or physiologic values of foods are permissible.

MASTICATION NOT AN AID TO "HEALTH" OF TEETH AND GUMS

Claims that the mastication of specific foods "keeps the teeth and gums clean and healthy" and equivalent statements are meaningless, misleading and deceptive by implication and are not permissible.

PREPARED FRUIT JUICES; LIQUID, FROZEN OR DRIED

Fruit juices, whether liquid, frozen or dried, shall be prepared and packed in such a manner as to preserve in the highest degree possible with the most efficient available commercial methods their natural vitamin values; products with materially reduced vitamin content shall bear appropriate and prominent declaration to that effect.

SULPHUR DIOXIDE IN INFANT FOODS

Small quantities of sulphur dioxide are permissible in fruit products specially prepared for infants or children, provided the quantity does not exceed that compatible with good manufacturing practice in the preparation of the dried fruit used.

TONIC CLAIMS

The term "tonic" or its inflected forms have vague and misleading meanings or implications in food advertising and are not permissible.

USES OF TERMS "STERILE," "STERILIZED" AND "STERILIZATION"

The terms "sterile," "sterilized" and "sterilization" shall be used in food advertising in their correct scientific significance only. Foods processed to be free of pathogenic organisms or to keep sound and wholesome are not necessarily sterile, i. e., free from viable micro-organisms.

VITAMIN AND MINERAL CONTENT OF SIEVED FRUITS OR VEGETABLES RECOMMENDED FOR INFANTS, CHILDREN AND FOR SPECIAL DIETS

Sieved fruits or vegetables prepared for the feeding of infants and children or for other special diets shall retain in highest degree possible with the most efficient available manufacturing methods the vitamin and mineral content of the raw fruits or vegetables; products with materially reduced vitamin or mineral content shall bear appropriate and prominent declaration to that effect.

VITAMIN CLAIMS IN FOOD ADVERTISING

Indefinite or general vitamin claims are vague, noninformative and misleading and do not permit a distinction between foods as sources of the respective vitamins. Vitamin claims shall stipulate the specific vitamin or vitamins present. Vitamins present in a food in insufficient quantity to contribute in any significant manner to the respective vitamins value of the diet do not warrant mention. It is desirable that warranted vitamin claims be expressed in appropriate terms indicative of the relative potency of the food as a source of the vitamins in the dietary schedule. Foods may be considered relatively as fair, good and excellent or rich sources of vitamins.

Representative examples of the respective sources of the vitamins follow:

A. Fair.....Green vegetables.
Good.....Tomatoes, whole yellow corn, hens' eggs.
Excellent.....Butter.

B. (B_1) Fair.....Lean muscle meat.
Good.....Heart, liver, kidney, eggs, milk, whole cereals, green vegetables.
Excellent....Wheat germ, asparagus.

C. Fair.....Raw pears.
Good.....Bananas, pineapple.
Excellent.....Raw vine-ripened tomatoes, grapefruit, lemons, oranges.

D. Fair.....Milk or butter.
Good.....Eggs.
Excellent.....Cod liver oil.

E. Fair.....
Good.....Whole wheat.
Excellent.....Wheat germ.

G. Fair.....Whole wheat, dried beans, soya beans.
Good.....Wheat germ, meat, green vegetables.
Excellent.....Dried yeast, milk, eggs, liver, kidney.

VITAMIN CONTENT OF TOMATO JUICE

Tomato juice shall retain in highest degree possible with the most efficient available manufacturing methods the vitamin content of the raw juice; products with materially reduced vitamin content shall bear appropriate and prominent declaration to that effect.

VITAMIN FORTIFICATION OF FOODS

Tentatively no objection is taken to the reasonable fortification of food products, whether intended for special diets, convalescents or general use, with vitamin concentrates or with natural foods rich in vitamins; provided that, should future authentic information disclose evidence of danger from excess of any specific vitamin in the diet or that fortification of common foods with certain specific vitamins is not entirely in the interest of public health, then objection will be taken to such fortification without prejudice to the present decision.

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SATURDAY, MARCH 26, 1932

NUTRITION AND PREGNANCY

Pregnancy has been defined as essentially a problem in nutrition at a time when the dominant metabolic forces are such as favor growth. According to Slemons,[1] the question as to the substances required for fetal nutrition may be answered in two ways. On the one hand we may infer the needs of the fetus from those of the new-born infant, which is sustained by its mother's milk, or, on the other hand, we may resort to the analysis of its body, on the fair assumption that the substances found in the fetus represent its requirements for growth. From information of this kind we conclude that there is no great difference between the fetus and the adult so far as the quality of the food they require is concerned: in their life processes they use the same organic and inorganic substances, which are always available in the circulating blood of the mother.

Experience in the study of the processes of nutrition leads to the inference that for the most part the various tissues and organs will assume and retain their normal chemical composition and fundamental morphologic structure quite regardless of the rate of their development. The "law of the minimum" comes into play in the sense that, among the substances nutritionally essential to growth, the one furnished to the organism in minimum amount (relative to the need for growth at a normal rate) will thereby determine the rate of growth, the organism growing only to the extent to which it can increase its size and at the same time maintain the normal composition of its kind. This means that organs and organisms as a whole may tend to "mark time" in their growth whenever there is a relative shortage of some essential in nutrition. It has been pointed out,[2] however, on the basis of recent studies, that there is need for discrimination in predicting the effects of different nutritional shortages on growth, and equally that we should be on our guard against a false sense of security in assuming that the absence of any appearance of stunting necessarily means excellence of nutritional condition throughout. Sherman and Booher[3] have shown in the case of animals that, with dietaries good in other respects but containing less than an optimal amount of calcium, growth in height and weight may (and usually does) occur at a normal rate. In fact, there may be every physical appearance of excellent nutrition, while the body is nevertheless growing up calcium poor, as shown in these experiments by actual analyses of the experimental animals.

In pregnancy the immediate source of supply for the growing fetus is the mother. Is the deposition of the inorganic components of the bones of the fetus modified materially by the nutritive history of the maternal organism? If it is, the fact should become apparent in the chemical make-up of the bones of the new-born infant. Booher and Hansmann[4] have recently reported the calcium and total mineral content of the tibias of a series of normal new-born infants, together with a study of the antepartum histories of the mothers. The complexity of the processes involved in the little understood deposition of the inorganic ingredients in the bones should be recalled. It is necessary, as Booher and Hansmann point out, that the calcium salts be present in suitable quantities in the fluid bathing the osteoblasts, which in turn necessitates certain equilibrium concentrations of calcium, phosphate and carbonate in the circulating blood and lymph. Robison[5] has shown that, in the carriage of calcium salts to the bone, a part may be played by a hexose monophosphoric ester which has been detected in blood and which forms soluble salts with calcium. Under the action of an enzyme present in ossifying cartilage this calcium salt is hydrolyzed, and calcium phosphate with a certain amount of carbonate is precipitated in the organic matrix around the osteoblasts. The rôle of vitamin D or its equivalent in irradiation of one sort or another in regulating the disposal of the essential ossifying elements must be borne in mind. Calcification of the skeleton may in some respect be modified by the secretions of certain endocrine glands, notably the pituitary and parathyroid structures. Bone, we are further reminded, is not a fixed product but an active ever-changing living tissue, the formation of which is regulated by a complexity of interrelated factors normally acting with precise coordination.

Bearing in mind these various factors that might be assumed to affect the degree of calcification of the skeleton of the new-born infant in its acquisition of inorganic elements, Booher and Hansmann analyzed tibias secured post mortem in the case of individuals

1. Slemons, J. M.: The Nutrition of the Fetus, New Haven, Yale University Press, 1919.
2. Calcium in Growth and Development, editorial, J. A. M. A. **97:** 1305 (Oct. 31) 1931.
3. Sherman, H. C., and Booher, L. E.: The Calcium Content of the Body in Relation to That of the Food, J. Biol. Chem. **93:** 93 (Sept.) 1931.
4. Booher, L. E., and Hansmann, G. H.: Studies on the Chemical Composition of the Human Skeleton: I. Calcification of the Tibia of the Normal New-Born Infant, J. Biol. Chem. **94:** 195 (Nov.) 1931.
5. Robison, R.: Biochem. J. **17:** 286, 1923. Robison, R., and Soames, K. M.: Ibid. **18:** 740, 1924.

born of mothers with greatly varied nutritional histories. Some had experienced the drains of pregnancies shortly before the one under investigation; some mothers were nourished far better than others; some were undoubtedly drawing on their own skeletons to meet the calcium demands of the growing fetus. A practically constant degree of calcification of the skeleton of the normal new-born infant was found, representing an exceedingly precise chemical coordination. The average proportion of calcium in the ash of the tibias was 37.4 per cent, with a small range of individual values. This is in all probability consistent with the finding that bones contain a crystalline mineral of the apatite series. Booher and Hansmann have concluded, therefore, that with respect to the deposition of the inorganic constituents of its bones the normal human fetus may be regarded as entirely parasitic on the maternal organism, since large differences in calcium and phosphorus intake by the mothers did not affect the degree of calcification of the tibias of the new-born infants. When the age of the younger mothers was such that active calcification of their own bones should have been taking place simultaneously, this had no appreciable effect on the calcification of the skeletons of the full term fetuses borne by them.

DRAINAGE FROM THE NASAL MUCOSA

The integrity of the organism is maintained not only through adequate nutrition but also through suitable protective devices. The outer layers of the skin containing keratin, the characteristic resistant protein, are admirably adapted to the function of protection. No less well suited for this purpose is the mucous membrane lining the gastro-intestinal tract and respiratory passages. In a recent study, Hilding [1] has contributed new facts bearing on the flow of mucous currents in the nose and the relation of the ciliated membrane to it. He points out incidentally that the typical secretion of the mucosa covers the nasal, pharyngeal, esophageal and gastric surfaces; it is like an unbroken membrane extending not only throughout the interior wall of the main tract but also into the sinuses. The beneficent action of the mucus in the mouth and in the stomach has long been recognized. Even in those species without the digestive enzyme ptyalin, the saliva is of great importance because of its lubricating action, which, in turn, depends on the mucus to no small degree. The gastric mucus undoubtedly serves as a protective mechanism against autodigestion, a point that is emphasized when local erosion occurs. Foreign bodies with points or sharp edges are rendered less harmful by the covering of mucus that accumulates as the object passes down the gastro-intestinal tract. To these better known facts, Hilding has added others of striking character.

Drops of india ink were placed on the membrane of various parts of the nose, and their movement was noted. The film of mucus in the nose and nasopharynx is continuously moving, at a rate which varies in different parts of the nasal cavity and in the general direction of the nasopharynx. This movement results from the force of gravity, from the pull of swallowing and directly or indirectly from the action of the cilia of the mucous membrane. The anterior third of the nasal mucosa shows relatively little ciliary activity and the movement of the mucous layer is slow in this region; it may require fifteen minutes or a half hour for it to move a few millimeters. However, when the mucus reaches the more active region posteriorly, movement is more rapid. The greatest ciliary activity appears to be in the meatuses; the mucus from the anterior part passes diagonally down into the meatuses and is rapidly transferred to the lateral walls of the pharynx. In the active region where the ciliary movement is pronounced, the mucus passes backward and downward with a tendency to drainage into the meatuses. Moving at the rate of from 4 to 6 mm. a minute, the drops of india ink traversed the distance from the anterior attachment of the middle turbinates to the opening of the eustachian tube in from four to ten minutes.

Like the lateral wall, the septum has an anterior zone that is inactive. In both structures this inactive area is where the inspired air first strikes the mucosa. If these currents of air are deflected by anatomic peculiarities, the inactive areas on the mucosa vary accordingly. The drainage from the septum is downward and backward to the posterior margin or to the upper surface of the soft palate. There is only a narrow inactive area at the anterior end of the floor of the nasal cavity. Ink deposited on the floor moved straight backward to the upper surface of the soft palate.

The physical character of mucus, together with its movement, constitutes an effective defense mechanism against attack by air-borne agents. The slimy, elastic, tenacious and pliable fluid layer catches and holds particles of dust, powder, pollen, bacteria and mold spores; the action of the cilia, directly in the active part or indirectly by traction in the anterior nasal cavity, moves the mucus posteriorly, to a large extent into the meatuses and thence to the pharynx, where it is removed by swallowing. Thus it happens that the deeper portions of the nose are comparatively sterile. The acidity of the gastric juice is a further device whereby the swallowed material is rendered innocuous, if not sterile.[2] It is well to remember that the mucous membranes of the gastro-intestinal tract and respiratory passages are in effect external body surfaces, as well adapted to protection in their location as is the skin in its situation. The mucus deserves greater respect and consideration than it frequently receives.

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1. Hilding, A.: Arch. Otolaryng. **15**: 92, 1932.

2. Johnson, T. M., and Arnold, L.: Proc. Soc. Exper. Biol. & Med. **29**: 501, 1932.

DEGENERATIVE ARTHRITIS—IS IT A SEPARATE DISEASE?

Arthritis as a disease of uncertain etiology is obeying the law that history repeats itself. As in the case of most other diseases, arthritis has gone through a long period of clinical observation and therapeutic trial and error. Numerous theories have been advanced concerning the etiology, some of them apparently inadequately controlled. Following Nichols and Richardson's anatomicopathologic studies [1] there has been a general lapse in consideration of the fundamental pathogenesis, punctuated at intervals by a recrudescence of interest.

Because of the marked difference in anatomic end-changes between a degenerative (hypertrophic) arthritis and proliferative (chronic infectious) arthritis, many students are inclined to assign an entirely different set of etiologic factors to the two types of joint disease. Others have questioned the soundness of this view. The recent work of Klinge,[2] therefore, is of considerable possible significance in determining this question. The first step in Klinge's experiments was to sensitize rabbits intradermally to horse serum. Then from 0.25 to 1 cc. of horse serum was injected into one knee joint, there producing an acute inflammatory reaction. During the course of five months a similar quantity was injected intra-articularly nine times into each of the rabbits. The animals were killed at varying intervals following the injections, and careful histologic studies were made of the injected joints. The acute joint changes, resembling in some respects those of rheumatic fever, were described by Klinge [3] in earlier communications. The gradual subsidence of the acute changes to subacute were described by Klinge and Fricke.[4] It remained to follow the aseptic inflammatory process into the chronic degenerative process, and this Klinge has done by allowing his animals to live from one to three years after the acute inflammation. The injected joints were examined roentgenographically at intervals and they showed the development of typical hypertrophic bony changes. Histologically the early and late stages of bony spurring and lipping were also characteristic. Curiously enough the opposite knee, which had never been injected, showed similar changes, but to a much less marked degree. This was true in the roentgenograms and microscopically. The explanation offered for this by Klinge was that the state of general sensitization to horse serum allowed a less acute allergic inflammation in other joints than in the one injected.

The chronic joint changes in rabbits following aseptic allergic inflammation are intriguing because of the possible relation to the pathogenesis of arthritis in man. There have been numerous studies [5] during the last few years on the relation of allergy and rheumatic fever, but with few exceptions [6] this interest has not been carried to the more chronic joint diseases. Klinge's experiments, if confirmed by others, will seem to prove that the end-results of provoking local inflammation in a joint with a foreign protein substance are marked bony changes which are indistinguishable from those of so-called hypertrophic arthritis in man. That this is the only means of producing such changes seems improbable. This lead, however, should be followed by other experimental studies. Special attempts should be made to determine whether it is allergic inflammation, or merely any inflammation, of joints which is followed by degenerative changes. It is also important to determine what particular tissue injury is responsible for these changes—vascular, synovial, cartilaginous, or bony. Certain it is that such studies as these by Klinge must be considered with deep interest by all those studying the pathogenesis of joint disease.

1. Nichols, E. H., and Richardson, F. L.: Arthritis Deformans, J. M. Research **21**: 149 (Sept.) 1909.
2. Klinge, F.: Experimentelle Erzeugung von Arthritis deformans, Verhandl. d. deutsch. path. Gesellsch., April, 1931.
3. Klinge, F.: Das Gewebsbild des fieberhaften Rheumatismus, Virchows Arch. f. path. Anat. **278**: 438, 1930; **279**: 1, 1931, and others.
4. Klinge, F., and Fricke, G.: Experimentelle Untersuchungen über anaphylaktische Entzündung der Gelenke, Krankheitsforschung **9**: 81, 1931.
5. By Swift and others.
6. For instance, Freiberg, J. A.: Allergy as a Factor in the Production of Proliferative Arthritis, Arch. Surg. **18**: 645 (Feb.) 1929.

Current Comment

AIRPLANES AND MOSQUITOES

In a reference to the progress made during the past half century in the field of public health in a representative New England city, Winslow [1] pointed out that the major health problems of the earlier days have been almost completely solved. The epidemic diseases, diphtheria, scarlet fever, typhoid and diarrheal diseases have disappeared as important factors in the death rate. Eastern municipalities may be finished with them, if current progress is maintained. The large and significant problems for the days to come appear to involve primarily pneumonia, cancer and the closely interrelated group of diseases of the heart arteries and kidneys. The importance of "eternal vigilance" to preserve the successes already attained is now and then emphasized anew by discoveries of new methods of disease transmission as a consequence of modern rapid transportation and world-wide travel. Old endemic centers of danger, notably in the tropics and in more than one continent, are being explored and opened to at least temporary residence by a floating population. Officers [2] of the U. S. Public Health Service have recently admitted that the possible importance of the aerial transportation of mosquitoes, particularly Aedes aegypti, has been a matter of serious interest to public health officials for several years. With steady increase in passenger traffic by air, the establishment of airlines connecting practically all countries, and the ever increasing speed with which air travel is being accomplished, the hygiene of the air transport service calls for careful consideration. Investigations recently made on passenger-carrying airplanes indicate that they are capable of harboring and carrying mosquitoes. Specimens of

1. Winslow, C.-E. A.: Health, Monthly Bulletin, New Haven Department of Health **58**: 8 (Nov.) 1931.
2. Griffitts, T. H. D., and Griffitts, J. J.: Mosquitoes Transported by Airplanes: Staining Method Used in Determining Their Importation, Pub. Health Rep. **46**: 2775 (Nov. 20) 1931.

both the Aedes and Culex species have been found on planes traveling between South American and Central American ports and this country. Griffitts concludes that, with conditions at airports such as would permit many mosquitoes to get aboard, it might be expected that approximately one fifth of the original number would be transported for a long distance—at least 1,250 miles—in one day, with repeated landing and the opening of doors, hatches and windows, and refueling, unloading and loading taking place. Under average natural conditions of mosquito production about airports, heavy infestation of aircraft would not be expected and, consequently, mosquitoes in only small numbers would make the trip. However, even a few infected, or infective, Aedes aegypti mosquitoes might be the means of starting an epidemic. Notwithstanding the fact that airplanes may, or do, transport mosquitoes, the government experts believe that this mode of introduction of mosquito-borne disease is probably secondary in importance to the importation of infected man. The transport of vectors of infection by aircraft is at most a potential danger. It needs merely to be appreciated in order to be properly controlled.

TUBERCULOSIS IN MEDICAL STUDENTS

One of the characteristic features of modern movements in public health is the greater attention now being devoted to preventive medicine in our schools, colleges and universities. Well equipped departments of health in universities and similar organizations for promoting the development and physical well being of American students—both young men and young women—are now found in most progressive educational institutions. Health examinations of students have become the rule. Unsuspected defects are thus disclosed during the period of adolescence and somewhat later; slight impairments of health are detected and managed; personal hygiene is promoted through the advice of special physicians; and possible impending disasters may be discovered in their incipience and thereby averted. It would be a symptom of optimism to imply that this beneficent movement has made more than a good beginning. If there is any place where the doctrine of a sane mind in a sound body should find ready acceptance it is in our seats of learning—places where the organized common sense of the sciences should find vigorous promotion without debate. However, human nature is much the same everywhere. All too often it requires ill health to supply the incentive to practice hygiene. As a recent writer expressed the situation, the man who is most receptive on the subject of health conservation is, in the majority of cases, the man who has just had some ominous warning of coming ill health. Of all the places where the traditional indifference should be overcome, the schools of medicine rank first. They are engaged quite as much nowadays in promoting a knowledge of prevention of disease as in effecting cures or affording relief to the disabled. Lately the health of medical students in the United States has been under careful consideration. Are the medical schools overlooking the health problems under their very eyes? A recent record from one of them by a group of competent examiners [1] indicates that the incidence of tuberculous infection, to cite an illustrative case, gives occasion for reflection. Examinations to discover the frequency of tuberculous infection were made of 279 premedical college students and of 452 medical students and were compared with similar examinations of boys attending high school. Tuberculous infection indicated by the tuberculin test increased with age, occurring in 77.8 per cent of the high school boys, in great part between the ages of 15 and 18 years, in 85.6 per cent of the premedical college students, largely between the ages of 16 and 21 years, and in 93.6 per cent of the medical students, largely between the ages of 21 and 26 years. According to the Philadelphia clinicians,[1] so far as tuberculous conditions are concerned, an increasing frequency of grave infection during adolescence and early adult life is evident, but no comparable data are available concerning the occurrence of tuberculosis in young men pursuing other occupations and presumably in good health. Nevertheless, the high incidence of apical lesions in these medical students, increasing rapidly from the ages of 21 to 26, indicates that they were peculiarly subject to advanced tuberculous infection. Here is a problem for scientific medicine within its own gates.

1. Hetherington, H. W.; McPhedran, F. M.; Landis, H. R. M., and Opie, E. L.: Tuberculosis in Medical and College Students, Arch. Int. Med. 48:734 (Nov.) 1931.

Association News

THE NEW ORLEANS SESSION

Railroad Transportation to New Orleans

Up to this time, information has been received that the Southeastern Passenger Association and the Central Passenger Association have granted a rate of one and one-half fares for the benefit of the members of the Association who will attend the annual session, to be held in New Orleans, May 9 to 13.

In order to secure the reduced rate it will be necessary for members to have a Certificate, to be endorsed by the Secretary of the Association and validated by a representative of the railroads at the Registration Bureau. These Certificates must be secured from railroad ticket agents at the time tickets to New Orleans are purchased. The Certificates, when properly certified by the Secretary of the Association and validated by the agent of the railroads, will entitle the holders to purchase return tickets, over the same route traveled to New Orleans, at one-half the regular fare. The reduced rate cannot be secured without a properly certified and validated Certificate.

MEDICAL BROADCAST FOR THE WEEK

American Medical Association Health Talks

The American Medical Association broadcasts on Monday from 12 noon to 12:05 p. m. over Station WBBM (770 kilocycles, or 389.4 meters) and other stations of the Columbia Broadcasting System, and on Wednesday and Friday from 2:25 to 2:30 p. m. over Station WBBM, Chicago.

The program for the week is as follows:

March 28. Diet on the Farm.
March 30. How Do Your Children Rate You?
April 1. Stretching the Food Dollar.

There is also a fifteen minute health talk sponsored by the Association on Saturday from 11:15 to 11:30 a. m. over Station WBBM, Chicago.

The program for the week is as follows:

April 2. The Three Weary Todds.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ALABAMA

Society News.—The northwestern division of the Alabama Medical Association was addressed at University, January 31, among others, by Drs. Charles E. Abbott, Jr., Tuscaloosa, on "Early Tuberculosis in Children," and Ralph McBurney, "Nutrition in Relation to Dental Health."——The Houston County Medical Society was addressed, January 8, by Drs. Frank K. Boland and Murdock S. Equen, Atlanta, on "Surgery of the Tuberculous Chest" and "Removal of Foreign Bodies from the Esophagus and Trachea," respectively.——Dr. Lemuel B. Nicholson, Gadsden, addressed the Marshall County Medical Society, January 13, on "More Common Upper Respiratory Conditions."——Dr. Thurston D. Rivers, Montgomery, clinician in the division of tuberculosis control of the state department of health, resigned, February 1, to enter private practice.

State Medical Meeting.—The sixty-fifth annual session of the Medical Association of the State of Alabama will be held at Mobile, April 19-22, under the presidency of Dr. Marion Toulmin Gaines, Mobile. The guest speakers, according to the preliminary program, will be Drs. Alton Ochsner, New Orleans, "Diagnosis and Treatment of Acute Intestinal Obstruction"; Jesse H. York, Atlanta, "Observations in Spinal Anesthesia"; Thomas B. Sellers, New Orleans, "Gynecology Office Equipment," and Edward H. Cary, Dallas, Texas, President-Elect, American Medical Association, "Obligations and Opportunities of Local Medical Men." Dr. Abernathy Benson Cannon, New York, will give the Jerome Cochran Lecture. Included among the Alabama physicians on the program are Drs. James Otis Lisenby, Atmore, "Increasing Mortality from Appendicitis"; John E. Walker, Opelika, "Bacteriophage: Its Nature and Therapeutic Application," and James N. Baker, state health officer.

COLORADO

Phipps Memorial Sanatorium to Close.—The Agnes Memorial Sanatorium, established in Denver in 1902, will cease to operate as a hospital for the treatment of pulmonary tuberculosis, July 1, and will not receive patients after June 1. The sanatorium is able to provide accommodations for 150 patients; at present there are forty-five patients under treatment. There are between fifty and sixty persons employed at the sanatorium. Although some of the buildings have been closed, the expense of maintaining the hospital when filled to less than one third of its capacity is no longer justified, it was stated. According to the deed of conveyance, the property must be used for charitable purposes, so it is not planned to close or abandon the buildings but to convert them to some other worthy purpose. Former Senator Lawrence L. Phipps established the institution as a memorial to his mother. When opened, it was the only one of its kind in Denver, it was stated, and the only other similar establishment was at Saranac Lake, N. Y. There are twelve buildings, erected at a cost of about $700,000, which are maintained on a forty acre site by an endowment also provided by Senator Phipps. The sanatorium was designed to furnish accommodations and medical attendance for persons of moderate means who have pulmonary tuberculosis. Dr. George W. Holden, medical director and superintendent, has been in charge of the institution since it was opened.

CONNECTICUT

Psittacosis Made a Reportable Disease.—At a meeting of the Public Health Council, January 21, psittacosis was made a reportable disease in Connecticut. The regulation became effective, February 20.

Society News.—Dr. Henry B. Richardson, New York, addressed the New Haven Medical Association, March 2, on "Study of the Tubercle Bacillus."——Dr. John C. A. Gerster, New York, addressed the Waterbury Medical Society, February 11, on "Surgeons' Problems in Gastric Surgery."

Personal.—The March issue of the *Yale Journal of Biology and Medicine* has been published as the "Mendel Anniversary Number" in honor of the sixtieth birthday of Lafayette B. Mendel, Ph.D., Sterling professor of physiologic chemistry, Yale University School of Medicine, New Haven. The Festschrift has as the frontispiece an engraving of a portrait of Professor Mendel and is made up of contributions by his pupils and associates. Professor Mendel was presented with the portrait of himself on his birthday, February 5 (THE JOURNAL, February 13, p. 359).——Dr. William J. Tate, Jr., Deep River, has been appointed health officer of Chester.

Two Counties Report 148 Cases of Smallpox.—Since December, 1931, and up until February 13, a total of 148 cases of smallpox had been reported to the state board of health from eight towns or cities in Fairfield and New Haven counties, according to the bulletin of the New Haven Department of Health. This outbreak mars the record covering a period of two and a half years, May, 1929, to December, 1931, during which there was not a case of the disease reported in Connecticut. Following are the cities reporting smallpox with the number of cases in each up to February 13: Bridgeport, 94; Stratford, 16; Trumbull, 12; Fairfield, 10; Seymour, 10; Shelton, 3; Milford, 2, and Danbury, 1.

IDAHO

Society News.—The Nez Perce County Medical Society was addressed, February 18, at Lewiston, by Drs. John C. Lyman on "Pancreatic Necrosis"; James T. Rooks, "Sarcoma of Antrum"; Roy A. Gunter, "Lung Diseases with Special Reference to Chronic Bronchiectasis"; Dr. Carl J. Johannesson spoke on the value of roentgen examinations in the conditions covered by his colleagues, demonstrated by x-ray films. All the speakers were from Walla Walla, Wash.

ILLINOIS

County Society Banquet.—Members of the medical and dental professions from McLean, LaSalle and Woodford counties were guests of the Livingston County Medical Society, March 17, at a St. Patrick's Day banquet. Dr. Earl V. Wilcox, Flanagan, president of the Livingston County Medical Society, acted as toastmaster. Mr. W. K. Lasher, Chicago, spoke on "The Business Side of Medicine and Dentistry."

Society News.—Dr. Vilray P. Blair, St. Louis, addressed the Adams County Medical Society, Quincy, March 14, on "Early and Late Treatment of Deep Burns."——The Peoria City Medical Society was addressed, March 15, by Drs. Russell L. Haden and Thomas E. Jones, Cleveland, on "Types and Treatment of Chronic Arthritis" and "Management of Neoplasms of the Colon and Rectum," respectively.——At the meeting of the La Salle County Medical Society, Mendota, March 17, the speakers were Drs. Thomas K. Brown and Isaac Y. Olch, St. Louis, on "Treatment of Puerperal Infection" and "Hyperparathyroidism and Hyperinsulinism and Their Importance in Surgery," respectively.——The Warren County Medical Society was addressed at Monmouth, February 19, among others, by Drs. Hermon H. Cole, Springfield, and James H. Hutton, Chicago, on "Diseases of the Chest" and "Recent Developments in Endocrinology," respectively.

Communicable Disease in Southern Illinois.—Six new nurses and a medical officer will be assigned by the state department of public health for duty in southern Illinois to assist a corps of three physicians and five nurses already in that area in a concentrated campaign of immunization against typhoid, smallpox and diphtheria. The special campaign will continue for three months, beginning April 1. The state department will also furnish free of local cost the necessary vaccines and toxoid. Last year the thirty-four southern counties experienced a distinctly higher prevalence rate of these diseases and of tuberculosis than did the central and northern thirds of the state. Cook County made the tuberculosis rate of the northern third a little higher than the southern, but, exclusive of Cook County, the northern third had a death rate from tuberculosis of 49.9, against a rate of 62 per hundred thousand in the southern third. There were seventy-three deaths from typhoid in 1931 in the thirty-four southern counties, giving a rate of 7.4, against a state rate of 1.6. Fifty-nine deaths were reported from diphtheria, giving a rate of 6, against a rate of 4.9 in the state at large.

Chicago

Society News.—The Chicago Society of Internal Medicine will be addressed, March 28, by Drs. Jesse R. Gerstley, on "Lactic Acid Milk: Has It Solved the Problem of Infant Nutrition?"; Carroll C. L. Birch, "Further Work on Hemophilia," and John A. Wolfer, "A Study of the Pancreatic Juice as a Factor in the Etiology of Gallbladder Disease."

Course for Laboratory Technicians.—Arrangements have been completed for making laboratory facilities at the Univer-

sity of Chicago, Division of Biological Sciences, available for training technicians. The essential feature of the plan is intensive training in special fields, no attempt being made to provide a generalized course in laboratory technic. Instruction will be practical, supplemented by library assignments, and after a preliminary period of intensive training the technician in training will be entrusted with a part of the routine work of the laboratory under careful supervision. Technicians will work in the laboratories without compensation, but no tuition will be charged. Training is offered in the clinical laboratory, serology, metabolism, electrocardiography, clinical chemistry, neuropathology, eye pathology and clinical bacteriology.

Racketeer Sentenced.—Jacob K. Karchmer, alleged racketeer, was found guilty, March 10, and sentenced, March 12, to serve two years in the federal penitentiary, having been convicted of mail fraud charges. Karchmer is alleged to have solicited donations through the mails for a babies' milk station, supposedly operated by the Volunteer Gospel Crusaders. Investigation carried on by the Chicago Association of Commerce showed that Karchmer's organization had only recently been incorporated and was dispensing a few quarts of milk a day, while Karchmer, through telephone and mail solicitation, was said to be collecting as high as $1,200 a week. Connected with this was Edward J. Salisbury, an optometrist, who is said to have admitted that he received $5 a week for the use of his name. Other legal difficulties in which Karchmer was involved are as follows: embezzlement, October, 1929; charged with using the mails to defraud, Feb. 8, 1930; indicted for conspiracy to defraud, Oct. 30, 1930. In every case up until 1932, he has been able to gain his freedom through legal technicalities. He has been called "Jake the Immune." Karchmer has filed a routine notice of appeal.

MARYLAND

Professor Waldschmidt-Leitz to Give Dohme Lectures.—Prof. Ernst Waldschmidt-Leitz, director, Institute of Biochemistry, Deutsche Technische Hochschule, Prague, will give the Dohme Lectures at the Johns Hopkins University School of Medicine, Baltimore, April 20-22. The titles of the lectures will be "Specificity and Mode of Action of Proteolytic Enzymes," "Structure of Proteins" and "Biological Significance of Enzymatic Activation."

Winter Clinics.—Dr. Russell Wilder, Rochester, Minn., with a clinical lecture on "Diseases of the Parathyroids," March 3, concluded the winter series of clinics given at the University of Maryland School of Medicine, Baltimore. For ten years the university has held a series of late Thursday afternoon clinics for the practitioners of Baltimore and vicinity. About one half of the guest clinicians are connected with the faculty of Johns Hopkins University Medical School. The out-of-town clinicians in the series just ended were Drs. William D. Stroud, Philadelphia, cardiovascular clinic; Walter M. Simpson, Dayton, Ohio, "Recent Developments in Undulant (Malta) Fever"; Ray W. Matson, Portland, Ore., "Surgical Treatment of Pulmonary Tuberculosis," and Edward Francis, Washington, D. C., "Tularemia." The Baltimore physicians included Drs. Lewellys F. Barker, John C. Gittings, John M. T. Finney, Thomas R. Boggs, Charles R. Austrian and Walter E. Dandy.

Prenatal Clinics.—Forty-eight prenatal clinics were held during 1931, under the joint direction of the state department of health and the local health departments in the five counties in which such conferences have been organized, according to the state department of health. They were attended by 142 expectant mothers, 88 white and 54 colored, who made a total of 298 visits to the clinics. Prenatal clinics are established in Havre de Grace, Harford County; Elkton, Cecil County; Cumberland, Allegany County; Prince Frederick, Calvert County, and Anne Arundel County. In each instance, the conference was established at the request of the county health officer with the approval of the practicing physicians of the county. All the patients either were referred to the clinic by their own physicians or were indigent patients who had made no obstetric engagement. The deliveries were conducted by local physicians either in the homes of the patients or in nearby hospitals. Wassermann tests and urine examinations were made by the laboratory of the state department of health for each patient.

MASSACHUSETTS

Personal.—Dr. Edward Reynolds recently resigned as director of the Peabody Museum of Achaeology and Ethnology of Harvard University on account of ill health. Dr. Reynolds graduated from Harvard University Medical School in 1885. ——Dr. Lawrence J. Henderson, Cambridge, lectured at Harvard University Medical School, March 8, on "The Influence Galileo on Medical Science."

Public Meetings on Cancer.—The Massachusetts Department of Public Health will conduct public meetings on cancer in fifteen cities and towns of the state during the week beginning April 4. The curability of the disease will be emphasized in discussions of diagnosis and treatment. The speakers will include Drs. Ray Lyman Wilbur, Secretary of the Interior, Washington, D. C.; Joseph Colt Bloodgood, Baltimore; James Ewing, New York; Robert B. Greenough and Channing C. Simmons, Boston, and Clarence C. Little, LL.D., New York.

Dr. Armstrong Gives Cutter Lecture.—Dr. Charles Armstrong, National Institute of Health, U. S. Public Health Service, Washington, D. C., will give the Cutter Lecture on Preventive Medicine, March 31, at Harvard University Medical School. His subject will be "The Complications of Smallpox Vaccination." These lectures are given annually under the terms of a bequest from John Clarence Cutter, whose will provided that they should be delivered in Boston free to the medical profession and the press. The medical profession, medical and public health students, the press and others interested are invited to attend.

MISSISSIPPI

Society News.—Dr. Oscar W. Bethea, New Orleans, addressed the East Mississippi Medical Society at Meridian, February 18, on "Diseases of the Chest." Drs. William R. Hand, Philadelphia, and Shields Abernathy, Memphis, Tenn., spoke on "Appendicitis in Children" and "Neglected Lesions of the Uterine Cervix," respectively.——At the meeting of the Issaquena-Sharkey-Warren Counties Medical Society, February 9, Vicksburg, the speakers included Dr. George M. Street on "Carcinoma of the Cervix." Speakers at the meeting, March 8, were Drs. Augustus Street, on "Management of Gallbladder and Biliary Tract Disease"; Charles T. Edwards, "Gastro-Intestinal and Respiratory Symptoms Secondary to Sinus Disease," and John R. K. Birchett, Jr., "Riedel's Struma."

MISSOURI

Society News.—At the meeting of the Jackson County Medical Society, March 22, the speakers included Drs. Paul F. Stookey and Joseph S. Lichtenberg on "Reactions to Therapeutic Serums" and "Allergic Disease of the Eye," respectively.—— Dr. Arthur N. Altringer, Kansas City, addressed the Jasper County Medical Society, March 1, on "Significance of Tonsils and Adenoids."——The Kansas City Academy of Medicine was addressed, March 18, by Dr. Louis J. Karnosh, Cleveland, on "Insanities of Famous Men."—— Dr. Derrick T. Vail, Jr., and William Mithoefer, Cincinnati, were the speakers before the Kansas City Society of Ophthalmology and Oto-Laryngology, March 17. Their subjects included, respectively, "Hypermature Cataract—Its Prognosis and Treatment" and "Acute and Chronic Sinus Problems." The physicians also conducted clinics.——Rev. Alphonse M. Schwitalla, dean of the St. Louis University School of Medicine, St. Louis, was elected president of the Missouri Social Hygiene Association at its annual meeting, February 11, and Dr. Richard S. Weiss, St. Louis, was made secretary.——The St. Louis Medical Society was addressed, March 15, by Mr. E. H. Bartelsmeyer on "Our Activities Relating to Medical Economics," and Dr. Rosco G. Leland, Chicago, "Some Phases of Medical Economics."——The Marion County Medical Society was addressed, February 26, by Drs. Charles H. Evermann and Clinton W. Lane, St. Louis, on allergy and precancerous lesions of the skin, respectively.——Dr. Jacob Geiger, St. Joseph, emeritus professor of surgery, St. Louis University School of Medicine, was host to the Buchanan County Medical Society at a dinner, March 2. The occasion was the celebration of the sixtieth anniversary of Dr. Geiger and the fiftieth anniversary of Dr. John B. Reynolds in practice in St. Joseph. Dr. Geiger was dean and professor of surgery of the Ensworth Medical College, St. Joseph, from 1883 until it closed in 1914.

NEW JERSEY

Health at Trenton.—Telegraphic reports to the U. S. Department of Commerce from eighty-three cities with a population of 36 million for the week ended March 12 indicated that the highest mortality rate (23.2) appeared for Trenton and the rate for the group of cities as a whole, 13.4. The mortality rate for Trenton for the corresponding week of 1931 was 18.5 and for the group of cities, 13.8. The annual rate for the eighty-three cities for the ten weeks of 1932 was 12.4, as against a rate of 14.2 for the corresponding period of last

year. Caution should be used in the interpretation of weekly figures, as they fluctuate widely. The fact that some cities are hospital centers for large areas outside the city limits or that they have large Negro populations may tend to increase the death rate.

NEW YORK

Society News.—Dr. Frederick C. Kidner, Detroit, addressed a meeting of the Buffalo Academy of Medicine, March 2, on "Industrial Back Injuries."——The Herkimer County Medical Society held a meeting, February 9, in Herkimer, in honor of Dr. William D. Garlock, Little Falls, who had completed fifty years of practice.——A symposium on tuberculosis was held at the meeting of the Medical Society of the County of Albany, March 22, by the following speakers from Mount McGregor: Drs. Edgar M. Medlar, pathology; Benjamin F. Seaman, studies of the leukocyte count; Gilberto S. Pesquera, value of the leukocyte count, and William H. Ordway, diagnosis and treatment.

Personal.—Dr. Livingston Farrand, Ithaca, N. Y., has been appointed a member of the Public Health Council by Gov. Franklin D. Roosevelt.——Dr. George A. Smith, superintendent of the Central Islip State Hospital for the Insane, completed fifty years in the service of the state, February 26. He entered the service as assistant physician in the Manhattan State Hospital and after serving thirteen years was appointed to establish the Central Islip institution, where he has remained continuously for thirty-seven years.——The Chancellor's Medal of the University of Buffalo was awarded to Frank A. Hartman, Ph.D., professor of physiology, at the midwinter commencement, February 22, in recognition of his work on Addison's disease.

New York City

Personal.—Dr. George Packer Berry of the Rockefeller Institute for Medical Research has resigned to become professor of bacteriology and assistant professor of medicine at the University of Rochester School of Medicine.——Dr. Jacob M. Gershberg was the guest of honor at a dinner given by the auxiliary of the International and Spanish-Speaking Association of Physicians, Dentists and Pharmacists, February 19, the fourth anniversary of the founding of the society. Among other speakers, Dr. George Draper made an address on the history of infantile paralysis. Dr. Gershberg is the founder of the society.

Koba Goes to the Penitentiary.—Lawrence Tsuneyoshi Koba, alias Tsuneo Kuba, pleaded guilty to attempted forgery in the third degree in the Court of General Sessions, New York County, Part 6, before Judge Morris Koenig. He was sentenced to the penitentiary on February 16. This being his first conviction, it is for an indeterminate period. The case of Koba, alias Kuba, was the subject of an article in the Bureau of Investigation department of THE JOURNAL, Aug. 1, 1931, in which it was brought out that Koba had displayed forged credentials from Johns Hopkins University, including a forged diploma. It is reported that in the present case efforts were made through the attorney general, Mr. Sol Ullman, to obtain the forged diploma and several postponements were given in order to get Koba to produce the document, but he made one excuse after another until the court sent him to the penitentiary. Efforts will be made through the parole board to get this document.

OHIO

Society News.—Drs. George T. Harding, Jr., and George T. Harding III, Columbus, addressed the Muskingum Academy of Medicine, Zanesville, March 2, on "Intoxication Psychoses and Bromides" and "Psychoneuroses," respectively.——Dr. Clifton F. McClintic, Detroit, addressed the Clark County Medical Society, Springfield, February 24, on headaches.——Seven Lima physicians presented a symposium on arthritis before the Four-County Medical Society (Defiance, Fulton, Henry and Williams counties) at Bryan, February 18, as follows: Drs. Burt Hibbard, Glenn E. Jones, Ralph O. Ruch, Fred G. Maurer, Gail E. Miller, Edward B. Pedlow and James W. Halfhill, Jr.——Dr. Wilhelm H. Vorbau, Lima, addressed the Van Wert County Medical Society, February 2, on "Mental Health and the Relation of Psychic Symptoms to General Medicine."——Dr. Roy R. Reynolds, Massillon, presented a paper on "Nasal Sinuses and Focal Infection" before the Tuscarawas County Medical Society, Dover, February 11.——Drs. William James Gardner and Bernard H. Nichols, Cleveland, addressed the Columbus Academy of Medicine, February 1, on tumors of the brain.——Dr. Philip J. Reel, Columbus, addressed the Ross County Academy of Medicine, February 4, on "Clinical Aspects of Uterine Fibroids."——Dr. Clarence J. Derby addressed the Montgomery County Medical Society, Dayton, March 18, on acute appendicitis.

PENNSYLVANIA

Anniversary of Public Health Department.—The January-February issue of *Pennsylvania's Health*, official journal of the state department of health, marks the twenty-fifth anniversary of the department. Five physicians have served as secretaries: the late Dr. Samuel G. Dixon, from the creation of the department until 1918; Dr. Benjamin Franklin Royer, Philadelphia, acting secretary, 1918-1919; Dr. Edward Martin, 1919-1923; Dr. Charles H. Miner, Wilkes-Barre, 1923-1927, and the present officer, Dr. Theodore B. Appel, Lancaster, appointed in 1927.

Discussion of Economic and Social Problems.—The meeting of the Allegheny County Medical Society, Pittsburgh, March 15, was devoted to economic and social problems of medicine, with the following speakers: Dr. Howard G. Schleiter, "Trends in Present-Day Medicine: Where Do They Lead Us?"; Mr. Lester H. Perry, executive secretary of the society, "The Problem of Medical Charity in Allegheny County"; Mr. Abraham Osseroff, director of Montefiore Hospital, "The Physician's Part in Hospital Free Work"; Dr. Raleigh R. Huggins, dean, University of Pittsburgh Medical School, "Upon Whom Shall We Depend for a Solution of the Dispensary Problem?" and Mrs. Helen Glenn Tyson, deputy secretary of welfare, state of Pennsylvania, "Medical Social Work: Where Does It Belong?" Drs. Milton B. Cohen, Cleveland, and Alexander H. Colwell led discussion of the addresses.

Philadelphia

Dr. Rowntree to Head New Institute for Research.—Announcement is made of the establishment of an institute for medical research in Philadelphia, to begin work in the autumn under the direction of Dr. Leonard G. Rowntree, now director of clinical investigation, Mayo Clinic, Rochester, Minn., and professor of medicine, University of Minnesota. The Philadelphia Institute for Medical Research will center its activities in the Philadelphia General Hospital and will attempt to foster research through affiliation and collaboration with all medical institutions in the city. It will afford a meeting place for all the medical school services at present affiliated with the hospital and will in addition hold itself ready to cooperate with any or all other institutions desirous of establishing a relationship. A site on the hospital grounds has been assigned for the erection of a building when funds become available, but in the beginning the institute will occupy temporary quarters in a new building now under construction and will function in conjunction with the hospital staffs. The new institute will be devoted to clinical investigation. Research will be made for methods of preventing disease, for improvements in methods of study, and of diagnosis and treatment, especially in the earlier stages. Studies will also be carried on in the fundamental branches of sciences underlying medical knowledge. According to the announcement, the creation of the Philadelphia Institute for Medical Research grew out of a centenary celebration of the birth of Pasteur in 1922 arranged by a group of Philadelphia physicians. Charter members of the institute were the late Dr. William Duffield Robinson, Admiral William C. Braisted, Dr. Judson Daland, the late Dr. Francis X. Dercum, Dr. McCluney Radcliffe, Provost Edgar Fahs Smith, Dr. Charles A. E. Codman, Mr. Hampton L. Carson and Mr. Joseph Carson. Dr. Daland is president. Dr. Rowntree, who has been appointed director, is a native of Canada and a graduate of the University of Western Ontario, London, 1905. Before going to Minnesota, he served several years on the faculty of Johns Hopkins University School of Medicine. In 1916 he became professor of medicine at the University of Minnesota School of Medicine and chief of the department. He has been associated with the Mayo Clinic since 1920. Dr. Rowntree has conducted research on renal function, acidosis and alkalosis, cirrhosis of the liver, arthritis and Addison's disease.

WASHINGTON

Society News.—Drs. Treacy H. Duerfeldt and Clyde Magill, Tacoma, addressed the Pierce County Medical Society, Tacoma, January 12, on "Asthma as an Allergic Disease" and "Chronic Prostatitis," respectively.——Dr. Ivan Glen Campbell, Vancouver, B. C., addressed the Puget Sound Academy of Ophthalmology and Otolaryngology, Tacoma, January 19, on "Sympathectomy in Retinitis Pigmentosa."——Drs. Edwin A. Nixon and Cassius H. Hofrichter addressed the King County Medical Society, Seattle, March 7, on "Parathyroid Tetany" and "Tooth Decay, Diet and Vitamins,"

respectively.——Dr. Karl H. Van Norman, formerly of Cleveland, has been named superintendent of Harbor View Hospital, Seattle.

GENERAL

Missouri Valley Society Meeting.—The Medical Society of the Missouri Valley will hold its annual meeting in Omaha, March 29-31. Among speakers who will appear are Drs. Walter C. Alvarez, Rochester, Minn., on "Recent Advances in the Science of Gastro-Enterology"; Henry F. Helmholz, Rochester, Minn., "Diagnosis and Treatment of Urinary Infections in Childhood"; Loyal Davis, Chicago, "Surgical Treatment of Trigeminal Neuralgia"; Joseph C. Bloodgood, Baltimore, "When Should Biopsy Be Done and How?" and Burt R. Shurly, Detroit, "A Research Study of Vitamins in Relation to the Defense Mechanism." In addition there will be a symposium on colitis, and clinics will be held each day. Dr. Bloodgood and Dr. Max Cutler, Chicago, will give a short course in pathology of cancer.

Senators Oppose Federal Aid to States.—Leading senators in debate on the Agricultural Appropriations Bill, March 3, condemned the federal aid policy. "Federal aid," declared Senator Carter Glass, Virginia, "is a misnomer; it is a miserable delusion. If the government would leave one tithe of the $114,000,000 that Virginia pays into the federal treasury in her own treasury, Virginia would not want any federal aid to good roads or good anything else." Senator David A. Reed, Pennsylvania, also opposed what he termed as "the sale of state rights in return for federal appropriations. . . . I do not like the types of legislation we have seen here in the maternity law, by which we tell the states how they shall have babies. I do not like a lot of this federal interference with local sovereignty and I think in the long run it heads us for disaster."

News of Epidemics.—Scarlet fever is reported to be epidemic in Philadelphia, 1,600 cases having occurred during January and February, the largest number since 1921. In New York 3,818 cases were reported between January 1 and February 25, as compared with 2,179 cases in the corresponding period of 1931.——Schools were closed for two weeks in Mount Vernon, Ohio, February 25, because of an outbreak of scarlet fever.——Five patients at the state hospital, Jacksonville, Ill., died of spinal meningitis during an outbreak in February; four were still sick, February 27.——Several cases of diphtheria were reported in Pueblo, Colo., in February, the first in two years.——There were 115 cases of smallpox in the public schools of Council Bluffs, Iowa, during January.——Epidemics of influenza in mild form caused the closing of schools in Dundee, Belding and Tustin, Mich., and 200 children were reported ill in Muskegon.——A case of leprosy was recently discovered in Moline, Ill., in a Mexican woman.

Society News.—The third International Congress of Eugenics will be held, August 21-23, at the Natural History Museum, New York. Information may be obtained from Mr. Harry H. Laughlin, Cold Spring Harbor, Long Island, N. Y.——The American Nurses' Association, the National Organization of Public Health Nurses and the National League for Nursing Education will hold their biennial joint convention in San Antonio, Texas, April 11-15. Among the speakers will be Dr. Clarence M. Hincks, director, National Committee for Mental Hygiene, New York, on mental hygiene as related to nursing.——Dr. Willis C. Campbell, Memphis, was named president-elect of the Southeastern Surgical Congress at its meeting in Birmingham, Ala., March 7-8. Dr. Gilbert F. Douglas, Birmingham, was elected vice president, and Dr. Benjamin T. Beasley, Atlanta, Ga., secretary, reelected. Dr. Frank K. Boland, Atlanta, became president. The next meeting will be held in Atlanta.——The National Congress of Parents and Teachers will hold its thirty-sixth annual convention in Minneapolis, May 15-20.——The eleventh annual meeting of the International Society for Crippled Children will be held at Rochester, N. Y., April 17-20.

Medical Bills in Congress.—*Changes in Status:* S. 1328 has been favorably reported to the Senate, without amendment, conferring on certain persons who served in the Quartermaster Corps or under the jurisdiction of the Quartermaster General during the war with Spain, the Philippine insurrection, or the China relief expedition the benefits of hospitalization and the privileges of the Soldiers' Homes. S. 572 has been formally reported to the Senate, with amendment, authorizing federal "cooperation" in promoting the health and welfare of mothers and infants (Senate Report 428). The following members of the Senate Committee on Commerce filed a minority report on the bill, protesting against the recommendation of the committee that the bill pass: Senator George H. Moses, New Hampshire; Senator Edwin S. Broussard, Louisiana; Senator Hubert D. Stephens, Mississippi; Senator Harry B. Hawes, Missouri; Senator Josiah W. Bailey, North Carolina; Senator Marcus A. Coolidge, Massachusetts; Senator Hiram Bingham, Connecticut, and Senator A. H. Vandenberg, Michigan. *Bills Introduced:* S. J. Res. 123, by Senator Jones, Washington, and H. J. Res. 335, by Representative Summers, Washington, to promote the conservation of health and education of minor children residing on tax-free Indian land on the Yakima Reservation, Washington, by authorizing the Secretary of the Interior to make expenditures therefor. S. 4109, by Senator Blaine, Wisconsin, to provide aid for Indians who are blind or deaf and blind. S. 4114, by Senator Reed, Pennsylvania, to transfer to the United States Public Health Service the division of vital statistics of the Bureau of the Census. H. R. 10584, by Representative Byrns, Tennessee, to prevent the sale or transportation in interstate and foreign commerce of any calcium arsenate, or lead arsenate or sodium fluoride without rendering such poison "distinct in color and appearance from any commonly used food or ingredient of food which it resembled in its natural condition." H. R. 10524, by Representative Celler, New York, to remove existing restrictions imposed on physicians with respect to the prescribing of spirituous and vinous liquor. H. Res. 168, by Representative Peavey, Wisconsin, to appoint a committee composed of members of the House Committee on Indian Affairs to investigate and study the health, education, and social welfare of the Indians of the United States.

Bequests and Donations.—The following bequests and donations have recently been announced:

St. Luke's Hospital, New York, and Loomis Sanitarium, Loomis, N. Y., are residuary beneficiaries of the estate of Emma Wade Scott, in the amount of $101,907 each.

Roosevelt Hospital, Nursery and Child's Hospital, New York Eye and Ear Infirmary, all of New York, $10,000 each under the will of Alice Shillito.

St. Mary's Hospital for Children, New York, $5,000 by the will of Mrs. Harriet M. Dickinson.

Hospital for the Ruptured and Crippled, New York, $50,000 from the estate of Mrs. Rebecca Witherell.

Dover General Hospital, Dover, N. J., $100,000, and Lenox Hospital, New York, $50,000 by the will of Paul Guenther, Dover.

Yonkers General Hospital, Yonkers, N. Y., $5,000 by the will of the late Mrs. Ann C. Arent.

Hahnemann Medical College Hospital, Philadelphia, $5,000 by the will of Mrs. Roas Rynning, Ocean Grove, N. J.

Jefferson, Babies', St. Agnes, Misericordia, St. Joseph's and St. Mary's hospitals, Philadelphia, $5,000 each; Hospital for Poor Consumptives and White Haven Sanatorium Association, White Haven, Pa., $25,000 to be applied on a new building, by the will of John F. Huneker, contingent on the death of his widow.

Addison Gilbert Hospital, Gloucester, Mass., $500 by the will of Octavius T. Howe.

Lowell General Hospital, Lowell, Mass., $250,000 by the will of the late Frank Hanchett.

Harlem Eye and Ear Hospital, $25,000, and St. Luke's Hospital, $15,000, by the will of the late William T. Koch.

St. Luke's, New York Foundling, Manhattan and St. Joseph's hospitals and Hospital for Ruptured and Crippled, all of New York, $10,000 each by the will of Giulia P. Morosini.

St. Joseph's Hospital, Providence, R. I., $5,000 for a free bed and $4,000 for the Hillsboro annex, by the will of Edith Lee Knowles Horton.

St. Peter's Hospital, Helena, Mont., $175,000 for a surgical unit, given by Mrs. Augusta Kohrs as a memorial to her husband, the late Conrad Kohrs.

The New York Orthopedic Dispensary and Hospital is one of five charitable institutions which will receive $1,134,334 each by the will of the late Mrs. Kate A. Harbeck.

St. Elizabeth and Elizabeth General hospitals, Elizabeth, N. J., and Overlook Hospital, Summit, $3,000 each by the will of the late Edward M. Burnett.

Montgomery Hospital, Norristown, Pa., $50,000 to be used for a children's ward, by the will of the late John Hoffman, Jr.

PHILIPPINE ISLANDS

Philippine Islands Medical Association.—Dr. Eusebio D. Aguilar was elected president of the Philippine Islands Medical Association at the twenty-ninth annual session, Dec. 15-18, 1931. Other officers elected were Drs. Tranquilino Elicaño and Gumersindo Garcia, vice presidents, and Antonio S. Fernando, secretary-treasurer. Acting Governor General George C. Butte was the guest of honor and Dr. Herminio Velarde, retiring president, made an address on "The Modern Trend of Health Administration." Among other speakers were Drs. Tomas M. Gan, on "Evolution of Preventive Medicine in the Philippines"; Juan Z. Santa Cruz, "Incidence of Amebiasis in Autopsies"; Aristeo R. Ubaldo, "Incidence of Cataract Among Filipinos"; Jose O. Nolasco, "Lymphatic Absorption of Oily Antileprotic Drugs, Intradermally and Subcutaneously," and Pedro T. Lantin, "Hospital Experience in Typhoid Fever in Filipinos."——The first regional medical convention of the Eastern Visayas and Northern Mindanao was held, Dec. 28-30, 1931, in Cebu, under the auspices of the Cebu Medical Society in conjunction with its annual session.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Feb. 22, 1932.

John Hunter

The oration in memory of John Hunter has been delivered at the Royal College of Surgeons for more than a century by the greatest surgeons of the day. Many of the later orators have expressed despair at being able to add anything to what has already been said, yet the large and distinguished audience that assembled to hear the Hunterian oration of this year, on "The Commemoration of Great Men," by Mr. Wilfred Trotter, expected a new and original treatment of an old theme and were not disappointed. While paying due tribute to Hunter's greatness, Trotter diverged from the usual oration by emphasizing Hunter's limitations, which, as he pointed out, were largely due to the period in which he worked. "Hunter was a consistent and expert user of the experimental method in the study of living processes, and it is on this fact that his fame essentially and ultimately rests. It was by impressing this method on his pupils and successors that his services to science and surgery have had their most extended and richest effects. These experimental studies covered a wide field and dealt with fundamental problems, such as the process of repair, the survival of isolated tissues, transplantation, grafting, inflammation, the processes of growth, and the influence on them of the sexual glands. Such researches were pursued with characteristic zeal and ability, and they yielded results of importance in many directions. It is impossible, however, not to be struck by a certain disproportion between the amount of energy and genius that was expended and the harvest of substantial knowledge that was gathered. Many of the researches were indecisive, not a few of the conclusions were incorrect, and no single advance was won which could be said to mark an epoch in the history of knowledge. Of Harvey, of Pasteur, of Lister, every student of physiology or pathology is in some sense the beneficiary and direct legatee. The influence of Hunter was more limited to the indirect and the germinal; he did not make an epoch; he founded a school." That Hunter's prodigious powers yielded such comparatively moderate accessions to knowledge might be explained by the fact that during his life (1728-1793) the biologist could not look for help to the sciences of the inorganic and was without the equipment now regarded as essential. When Hunter was in his prime, in 1765, oxygen had not been discovered and Joule's mechanical equivalent of heat and the compound microscope were far ahead.

Mr. Trotter passed to the more general subject of the commemoration of the great dead. At death a man entered into a new state, about which the only certainty was that it had nothing to do with life and his memory underwent a decline which nothing could arrest. In all our commemorations, whether by word or by plastic art, we made our own pictures and drifted increasingly away from the actual man. Perhaps a future age might reach the conclusion that the time to celebrate its heroes was while they were still alive. But unfortunately it was easier to recognize greatness after death when we were freed from the distraction of the actual presence, which tended often to be odd, angular and even quarrelsome. There was also the old story of the grudging and even hostile reception of new ideas. "The mind delights in a static environment. Change from without, interfering, as it must, with the sovereignty of the individual, seems in its very essence to be repulsive and an object of fear. How deeply rooted in the mind is the fear of the new. If mankind is to profit freely from the small and sporadic crop of the heroically gifted, it will have to cultivate the delicate art of handling ideas."

Returning to Hunter: "He lived in the relative intellectual freedom of the best part of the eighteenth century, before its bland sunshine had died down in the smoke of industrialism. He saw, as from a peak in Darien, the illimitable ocean of biology before him, and he addressed himself unhesitatingly to explore it all. It was in the general level of knowledge and in equipment that he was less fortunate. When a new Hunter appears, he will not be held back by an undeveloped science and he will find this college able to give him all the facilities with which it has been munificiently endowed."

The "Radium Bomb" to Be Withdrawn

The National Radium Commission, which controls the use of a large amount of radium, bought by public subscription, has decided to withdraw the 4-Gm. "radium bomb," provided at a London center, as the results were not satisfactory. This decision to remove the only source of mass radiation in Great Britain has evoked a protest in the *Times* from radiologists and surgeons who specialize in the use of radium. They contrast the position on the continent and in the United States. In Paris a 4-Gm. bomb is in use at the Institut de Radium. In Stockholm a 3-Gm. bomb has been in use for several years and the published results are excellent. The Memorial Hospital in New York has a 4-Gm. bomb in constant use. Brussels, which has had experience with a 4-Gm. bomb and with smaller units, is contemplating the construction of a 12-Gm. bomb. In Paris uterine cancer, in Stockholm cancer of the mouth and throat, and in New York cancer of the breast, as well as of the mouth and throat, are treated by mass radiation. It is true that in some cases the bomb is used in conjunction with other forms of radiation, such as radium needles, radium plaques and x-rays, but this in no way diminishes the value of the bomb. The signatories claim that certain types of cancer are better treated by the bomb than by any other method. By splitting up the bomb, all research into this form of radiation is being brought to an end in this country. They allege that a large number of surgical operations are still being done, which in view of the possibilities of radiotherapy are no longer justifiable. For these reasons they urge that a committee of inquiry be appointed by parliament to consider how best to advance radiotherapy, especially in its research aspects. While supporting this proposal, one surgeon, Mr. Donald Armour, asks, in defense of British surgeons, "On what grounds is the statement as to unjustifiable operations made?" Finally the presidents of the Royal College of Physicians and Surgeons (Lord Dawson and Lord Moynihan) have published a joint letter stating that the intervention of parliament is neither necessary nor desirable and that the duty of such an inquiry belongs to the medical profession.

The London Clinic and Nursing Home

The London Clinic and Nursing Home, the only institution of the kind on a large scale in this country, has been opened by the duchess of York. At the ceremony, the chairman, the duke of Atholl, said that the home was, for its size, unsurpassed in respect of equipment and modernity. It was hoped to provide people of moderate means with a fair and square deal. Lord Dawson (president of the Royal College of Physicians) remarked that it was a private hospital on a scale which, he thought, had not previously been reached, certainly not in London. Lord Moynihan (president of the Royal College of Surgeons) said that as far as the services which the medical profession had been able to render, the poor always received the best. The rich had had something which was almost but not quite the best; for it was essential for successful treatment that every method of investigation—clinical, pathologic, bacteriologic, radiologic—should be easily accessible under the same roof and that there should be immediate and complete opportunity for carrying out any indicated treatment. Such conditions had always existed in the large teaching hospitals, but the home in taking people of moderate means as well as the rich was making available a service which had not yet in

this country been offered to the class from which private patients come. The building covers 2½ acres and consists of 1,000 rooms on 10 floors and provides accommodation for 214 patients. The seventh floor, devoted to maternity cases, has a roof garden. There is a floor for children and another for special dietetic cases. There are seven operating theaters on the eighth floor.

Killed by a Feather

An inquest was held on a child, aged 5 months, who died under unusual circumstances. The child was under the care of a foster mother, who stated that it was well until one evening she heard it move and on going to the child, found it lying on its face and looking unnatural. When medical aid arrived, the child was dead. The necropsy was performed by the government pathologist, Sir Bernard Spilsbury, who said the child was a fine one and appeared to have been well cared for. He found a feather in the child's larynx and attributed death to laryngeal shock, which he said was rare. Apparently the child got the feather in its mouth and then inhaled it. Death was not attributed to asphyxia.

PARIS

(From Our Regular Correspondent)

Feb. 3, 1932.

Transactions of International Bureau of Public Health

The Office international d'hygiène publique, which has its headquarters in Paris, 195 Bld. St. Germain, and which is presided over at present by Mr. Abt, has published a report of the transactions of its October session, which brought together the official delegates of all the governments represented in this international organization, which is distinct from the health section of the League of Nations at Geneva. The communication contains a report on the course of epidemics throughout the world. As regards the plague, differences in the appreciation of the value of antiplague vaccination are noted, some of the opinions being favorable and some unfavorable. In Italy, the authorities have ceased to impose this vaccination on persons engaged in the unloading of infected vessels and in their deratization. Preference is given to passive immunization by means of three injections of serum, administered at ten day intervals in order to prevent serum sickness. Some reported a rather high proportion of cases of plague among the vaccinated, several of which proved fatal. On the other hand, the curative value of the vaccine in the pulmonary type of the plague, otherwise fatal, is recognized by all, especially if it is applied directly to the bronchi, in accordance with the technic of Dr. Nicolle of Tunis, by means of an atomizer. The conclusion is that one cannot list antiplague vaccination among the quarantine measures to be regularly recommended, because it does not prevent the propagation of plague by rats. There was in August an epidemic of cholera in Irak, with a mortality of 60 per cent, whereas in Shanghai the mortality ranged between 8.5 and 16.8 per cent, following numerous vaccinations. In India, the health authorities prefer to vaccination a wide distribution of the d'Herelle bacteriophage, which has given better results. A few cases of yellow fever were observed in Africa. Researches were carried out to test the possibility of mosquitoes being transported by airplane, with the result that it has been shown that mosquitoes die when the plane attains an altitude of 2,000 meters. An epidemic of hemorrhagic icterus was reported from the island of Syra, Greece, and an epidemic of exanthematic typhus in Rumania and in Athens. Smallpox had receded sharply in Great Britain and in America. The prophylaxis of malaria has made great progress with the use of plasmochin. Germany has strengthened the prophylaxis of syphilis by the introduction of an effective regulation concerning the treatment of sailors affected with venereal diseases.

Rectal Stenosis in Relation to Lymphogranulomatosis

Articles are appearing on a peculiar disease described by Nicolas Favre. Although one of its main characteristics is inguinal adenitis, numerous cases have been discovered in which the adenitis is lacking and in which the disease is diagnosed only by the intradermal reaction with the Frei antigen. Among these cases are lesions of the rectum the origin of which had not been determined. It was known that lymphogranulomatosis could produce such lesions, but one did not suspect lymphogranulomatosis in the absence of inguinal adenitis. Bensaude and Lambling applied the Frei test to twenty-one patients in the Hôpital St. Antoine, affected with rectal stenosis. All those who had at the same time inguinal adenopathy, whether suppurative or otherwise, gave a positive reaction. In a series of cases in which there were no inguinal or genital symptoms, the reaction was positive in twelve cases and negative in two cases. The twenty-one patients gave 90 per cent of positive reaction. Jersild had published previously reports of twenty-three cases, in which, however, there were genital symptoms. Bensaude called attention to the unexpected proportion of cases of simple and ordinary rectal stenosis in which lymphogranulomatosis was involved, although that fact was not suspected. According to Bensaude, the Nicolas Favre disease should be kept in mind in all cases of rectal stenosis, and the Frei test should be applied. On the other hand, Ravaut, together with Levaditi, Lambling and Cachera, discovered the presence of the virus of lymphogranulomatosis in a case of vegetative rectitis. Inoculations in the guinea-pig were made, which gave rise to inguinal adenitis. These glands introduced within the brain of the monkey produced the fatal meningo-encephalitis characteristic of lymphogranulomatosis. Furthermore, they served for the preparation of an antigen that enabled the examiner to obtain a positive Frei reaction in persons known to be affected with lymphogranulomatosis. The proof is thus furnished that this disease may produce rectal lesions of an indeterminate character, even in the absence of inguinal adenopathy, a result that is exceedingly important for the treatment of these lesions.

Direct Photography of Stomach Lesions

The technic of direct photography of stomach lesions has been improved. Victor Pauchet and A. Bécart reported recently the results in a communication presented to the Academy of Medicine. This method does not presume to replace other modes of gastric exploration, but it supplements them and facilitates the early diagnosis of the lesion by direct vision of the gastric mucosa. With a double metal camera introduced into the stomach by means of a semirigid sound of the diameter of a Faucher tube, the examiner can take sixteen stereoscopic pictures of nine tenths of the stomach in one one hundred and twentieth of a second. Ulcers and cancers can be recognized, whether located on the lesser curvature or on the two flat surfaces of the stomach. A number of cases that have come to treatment have served to verify the precision of the observations made of lesions with the aid of the apparatus. This constitutes a distinct advance. The authors reported fifteen cases in which the observations thus made were verified at the operation. A. Bécart projected on a screen eighty photographs of the stomach, which he had taken.

The Lannelongue Prize in Surgery

The Société nationale de chirurgie awarded, this year, the Lannelongue gold medal, bestowed every five years, for which the sum of 5,000 francs is provided. The prize is of international scope. The first medal was awarded to Sir Victor Horsley (Great Britain), the second to Mr. Henri Gaudier (France), and the third to Dr. Crile (United States). The prize was given this year to Professor Leriche of Lyons for research in physiology and surgery.

BERLIN

(From Our Regular Correspondent)

Feb. 1, 1932.

The Fate of Diabetic Patients

The large number of patients with diabetes (their number in Berlin is estimated at 8,000, and in all Germany at 100,000), who, on account of the long duration of their illness, make, on the average, the heaviest drain on the finances of the *krankenkassen*, causes the question as to their fate to be important from the standpoint of public health. In an address by Professor Umber, director of the department of internal diseases at the Krankenhaus Westend, before the Berliner Medizinische Gesellschaft, he emphasized that insulin (provided the dosage is carefully adjusted to the needs of the individual), in combination with a suitable diet, assures an "optimal, enduring result." In contrast with genuine pancreatic diabetes, there are other forms of sugar excretion that are harmless, that may cause temporary or long-continued sugar excretions and yet do not require dietary and insulin treatment; but the number of such cases is not large. In a series of 4,000 cases of diabetes reported from the Umber department, there were only 97 of these cases. About 90 per cent of all cases are genuine pancreatic diabetes. In these cases the carefully planned administration of insulin, together with the restricted diet, which, however, does not need to impair the happiness of the patients, determines their fate. In the 4,000 diabetic patients treated with insulin in his department, a permanently normal tolerance (recovery) was, to be sure, never attained, but permanent absence of sugar from the urine and complete physical and mental vigor and working capacity were secured. No substitute for insulin has been discovered as yet. Even diabetic coma, formerly so much dreaded, is successfully controlled by insulin without alkaline treatment, if the treatment is begun within eight hours after the onset of the coma, as is shown by observations on 195 such patients. Of 645 patients treated in the Umber department for patients with diabetes, in 1931, 4.3 per cent died, but only 1.2 per cent from diabetes, and then only because they had been brought to the hospital too late; that is, more than eight hours after onset of the coma.

Unfortunately, the diabetic patient is still compelled to inject the insulin that he requires. Insulin by mouth has practically no effect. Of all the widely advertised products that are supposed to cure diabetes through oral administration only synthalin or, better still, synthalin B of Frank, is effective. It permits utilization of from 20 to 30 per cent of the carbohydrates in the diet, but it is often poorly tolerated and is by no means a complete substitute for insulin. All other preparations were found, after testing at the Umber department for patients with diabetes, to have no effect. This statement of the author was not objected to in the discussion that followed his presentation.

With insulin it is possible to raise diabetic children who formerly were doomed to die—to prepare them thoroughly for an occupation and to make them worthy heads of families. Pregnancy and childbirth, severe illness, tuberculosis and surgical operations are withstood by diabetic patients properly treated with insulin just as well as by healthy persons. On the contrary, the additional risk involved when patients have slight disorders, as, for example, a "cold," is surprising, so that these conditions demand special attention. Nervous diseases have no demonstrable significance in diabetic disorders, and Umber is unable to find any evidence supporting the idea that diabetes may develop as the result of a trauma.

Important for the fate of diabetic patients is the care they receive after their dismissal from the hospital, where they followed a prescribed diet and received regularly the required amount of insulin. This after-care is just beginning to be organized. It is sometimes given by specially trained nurses, who visit these patients, give them regular instruction, and work hand in hand with the attending physician.

Great importance attaches also to the economic question. In spite of the great amount of study given to this matter, it is not yet possible to keep the costs of the diabetic diet and treatment as low as in other ordinary diseases. The liberal use of vegetables, fat and meat makes the diet of the diabetic patient somewhat expensive. This fact was emphasized, during the discussion that followed, by Professor Lichtwitz of the Virchow Krankenhaus, in these plain terms: "The fate of the diabetic patient depends, first of all, on the skill and judgment of his physician; secondly, on the understanding of the patient, and, thirdly, on the point of cost." In the metabolism centers of the hospital, patients are now often allowed to choose their food from a menu that offers several possibilities, without any additional cost of the treatment. This method has been of use at the Krankenhaus Westend and at the Virchow Krankenhaus, and has given entire satisfaction. The permanent diet of the diabetic patient will vary with the type of work and the number of hours that the patient is employed. Likewise the time of meals in the hospital should be governed by these criteria. According to Joslin of Boston, special importance attaches to the care of the feet and of the nails, with a view to preventing, as far as possible, diabetic gangrene.

CAPE TOWN

(From Our Regular Correspondent)

Feb. 1, 1932.

Anthropologic Investigations

Scientists in this country are a trifle tired of race theorists, whose postulates are so easy to controvert where examples of miscegenation are common. The Union of South Africa offers an admirable field for the investigation of ethnic problems, but so far no one has taken this research seriously. The universities have done nothing, and it remains for private enterprise to initiate such research. A privately financed expedition has arranged to report in the near future on the physique of native children in the aboriginal kraals—an investigation that should be of great interest and of real economic value. Dr. A. Pijper of Pretoria has now determined the blood groups of 615 aboriginal Bushmen and found these to be different from those of any other race in Africa. He maintains that this conclusion throws some light on the way in which the continent became populated. The Bushmen, according to his observations, have the most primitive distribution of blood groups of all African races and must therefore be the representatives of the first African colonists, who came from the Northwest, traveled right through Africa from north to south, and ended up by settling in the extreme southern end of the continent. The Negroes of middle Africa are serologically related to the northeastern tribes, while the Bantu, serologically considered, are the results of Hamitic invasions with a slight admixture of Negro blood. "To make the picture complete," he remarks, "one should add that the latest 'drift' into Africa has come from the south in contrast to all the others which came from the north, and that this latest 'drift' was, and still is, characterized by a distribution of blood groups exactly corresponding to that of western Europe." It may be added that Dr. Pijper's material came from the northern group of Bushmen, from the mandated territory of South West, and was taken chiefly from the Auen, Kung and Heikum tribes.

The Annual Medical Congress

It has been decided to hold the next medical congress at East London in June. East London at that time is a pleasant, mildly subtropical seaside resort. The date, however, interferes with the centenary meeting of the British Medical Association, which is to be held in July of this year in London. Many of our chief medicos intend to go to the centenary meeting and will therefore be unable to attend the medical congress at East London. Among those who are attending the London centenary meeting is the president of our association, Dr. J. Orenstein, who is going to Europe and America on long leave in March.

Dr. Orenstein has been president of the Medical Association of South Africa since its inception in 1926. This year his second term of office expires, and it is unlikely that he will allow himself to be renominated for a further three years. A new president and chairman of the federal council, therefore, will have to be elected from among the members of the federal council. There are several excellent senior men, but it is probable that the association's choice will be its vice president, Dr. Lindsay Sandes, a consulting surgical specialist and a lecturer on clinical surgery at the University of Cape Town.

Referendum on a Hospital Policy

The medical association has once more taken up the question of hospital policy in regard to the payment of honorary staffs. The matter has agitated the profession in this country for generations. The hospitals in the union are without exception state supported institutions, notwithstanding the fact that most of them are still staffed under the system that prevails in England, where the public hospitals are voluntary hospitals. This is due to the fact that the majority of physicians in this country were, up to a few years ago, English trained and came out with the English tradition of voluntaryism behind them, a tradition which many are still disinclined to surrender. Day by day, however, it is becoming increasingly apparent that the government and the local authorities are bent on exploiting the medical profession, and while to every one else the pauper is a ward of the state, for whom the state pays—sometimes extravagantly—when it comes to a question of disease and operation the physician is expected to give his services free to pauper patients. The profession has been dissatisfied with this state of affairs for long, and before now it has been made the subject of a referendum. These expressions of collective opinion have so far been indecisive, for they could be given only at meetings specially called to consider questions of policy. Now an alteration of the rules enables a postal vote to be taken on such matters and already it seems clear that the vote to be recorded on this occasion will be so far representative of professional opinion that the association can safely take it as a mandate. There is considerable difference of opinion as to whether payment of honorary staffs should be general or limited to certain smaller hospitals. There seems to be general agreement that where the honorary staff acquires a suitable recompense in teaching or advertisement, as in the case of the two large hospitals with medical schools attached, no payment should be asked for services rendered. The referendum is now being taken and its results will come before the federal council, which meets at the end of this month.

BELGIUM

(From Our Regular Correspondent)

Jan. 28, 1932.

The Colony of Mental Patients at Lierneux

The Société de médecine mentale de Belgique held a session recently at the colony of mental patients in Lierneux, when Mr. Massaut gave an account of this colony, in which mental patients are hospitalized in the families of villagers. The reasons for choosing the village of Lierneux for the colony were its distance from all centers, its absence of factories, its vast area (6,000 hectares), and its division into fourteen hamlets. The organizers wished to establish an experimental center for the care of mental patients; they desired to combine a familial colony, an asylum or retreat, an infirmary for intercurrent disorders and a lazaret for contagious diseases. The plan included general services: laundry, kitchen, store-rooms, offices, bathrooms and laboratories. The war interrupted the work, but the buildings and improvements were taken up again after the war closed. During the period 1924-1928, several pavilions and a necropsy room were added to the equipment. The number of patients in the colony at present is 567. Of these, 267 are placed in the homes of the villagers, while 300 are cared for in the retreat. The patients placed in the homes are selected cases. They take part in the family life; they work, and require only a minimum of supervision.

The 300 patients housed in the pavilions of the retreat are nearly all unoccupied. While the program as outlined has been realized to a great extent, the work must be further organized by the construction of workshops. It is hoped that soon a dressmaking shop for women and a shoe shop and a tailor shop for men will be available.

Mr. Massaut holds that the retreat in the colony should not be objected to. The experience at Lierneux shows that the two institutions can exist side by side and profit by collaboration.

The Protection of Native Industrial Recruits

The measures adopted in the Belgian Congo for the sanitary protection of the native man power were explained recently in detail to the committee of the international bureau of public health. Various organizations study the possibility of enlisting industrial recruits among the natives, the methods of recruiting, the transportation, the acclimatization and the sending of the workmen back home, and the supervision of the work as required by the employers. Three medical examinations are regularly made: one at the time of recruiting, one on arrival at the acclimatization camp, and one on arrival at the place of employment. At the acclimatization camp, a system of rational gymnastic exercises has been introduced, since the natives, with the exception of the hunters and the paddlers, are inclined to be narrow-chested. The creation of native quarters in the industrial regions, in which the natives own their own homes but not the ground, develops the family life and a sense of personal worth. The old custom of giving presents to the chiefs has been largely abandoned and, instead, payments are made to tribal funds, which are used to buy farming implements and medicines and to create dispensaries for trypanosomiasis patients, and leprosariums for natives. Health insurance societies to provide against industrial invalidity have been created to obviate the waste of money granted by the courts in the form of compensation for accidents. On the whole, the mortality of workmen in the service of white men is about the same as that recorded for the native villages. The mortality diminishes when the workmen are engaged for a longer period, as the factor of adaptation plays a big part.

The Franco-Belgian Sanitary Convention

The collaboration of Belgium and France in the Congo region has led to the drafting of a new convention concerning the measures to be adopted in combating epidemic and contagious diseases in their respective colonies. It is stipulated that the governments of French Equatorial Africa and of the Belgian Congo shall exchange, through the mediation of their medical services, monthly reports giving details of the manifestations, in their respective territories, of a stated list of diseases, to which, with common agreement, other diseases may be added from time to time.

Furthermore, the two governments may hold—sometimes in French and sometimes in Belgian territory—conferences of hygienists with a view to improving the system of health defense of the two colonies, and enabling the physicians to collaborate more intimately to that end. In the interval between the sessions, the physicians of the frontier regions will communicate to one another all necessary information and will hold meetings whenever an exchange of views shall seem desirable.

There will be established in the border areas a chain of medical stations as close together as possible, and measures will be taken to prevent, as far as possible, the passage, from one colony to another, of persons affected with a contagious disease or coming from infected zones.

The governments instructed their medical services in the frontier regions of the two territories to give careful attention to smallpox vaccination, to the treatment of trypanosomiasis, to the measures designed to destroy dangerous insects, to the census, to the treatment of leprous patients, and, in general, to

all measures calculated to prevent the transfer of infection from an infected to a noninfected area. Furthermore, the two administrations will endeavor to coordinate their efforts in all respects. The services will be asked to furnish information in regard to the itinerary to be followed by the physicians in the frontier zones, in order that such supervision may be simultaneous, as far as possible.

The Belgian and French physicians will find in this mutual aid new means of action that will enable them to bring the black race more extensive and more effective help.

The Franco-Belgian convention is the last, in point of time, of the conventions promoted by Dr. Trolli, chief physician of the Congo region. He had previously entered into similar conventions with the English and the Portuguese. The Congo region is thus entirely "girded about" at present.

NETHERLANDS

(From Our Regular Correspondent)

Jan. 28, 1932.

Rats as Transporters of Weil's Disease

Dr. D. J. Hulshoff, inspector of public health, and Dr. J. P. Anemaet have an article in the *Nederlandsch Tijdschrift voor Geneeskunde* on rats as the cause of contagion in Weil's disease. In the laboratories, 109 cases were carefully studied. There was a recrudescence during the period from 1924 to 1929, explainable possibly less by any increase in the incidence than by the fact that the disease become notifiable in 1924, and thus the attention of physicians was called to it. Rats were caught, especially at Gouda, a city near several bodies of water, and 196 rats were examined, 30 of which appeared to be infected. In 1929-1930, the six months of winter revealed that 8 per cent of the rats examined were infected. In 1930, the six summer months gave a percentage of 13, and October, November and December a percentage of 25. The total of 196 rats, with 30 rats infected, gave a percentage of about 15. It will be observed that the percentage of infected rats is about the same in summer and in winter, from which fact it is evident that the retiring of the sick rats to their holes does not influence the propagation of the disease. It is assumed that in the rats infection takes place from their eating food that has been contaminated by infected water. One method of combating the disease consists in using precautions in connection with outdoor bathing. Such precautions applied in the commune of Gouda brought about a marked diminution in the number of cases of Weil's disease, although the infection among rats persisted. The conclusions reached are that: 1. Infection among rats in Gouda with Leptospira icterohaemorrhagiae or Leptospira icterogenes has remained stationary since 1927. 2. The disappearance of the disease at Gouda is due to the installation of baths that are not contaminated by rats. 3. The seasons have no influence on the contagion in rats. 4. What is needed is the discovery of some means of constructing, at a reasonable cost, adequately protected baths or of transforming old bathing establishments into protected ones. 5. If such action is taken, the destruction of rats will no longer be necessary.

Aid for Unmarried Mothers

Recent public health reports contain interesting data on aid rendered to unmarried mothers. These are divided into four groups: (1) the indigent, for whom the costs of medical treatment and confinement are paid; (2) the needy, to whom aid is given by the charitable organizations if the resources of their family do not suffice; (3) prostitutes, most of whom do not need aid, and (4) workers, who are not permitted to engage in outside employment for two weeks before and six weeks after confinement. The commission considers that the six weeks of convalescence provided by the labor law is insufficient for unmarried mothers. The number of illegitimate births in 1929 was 3,322. The proportion of illegitimate children in 1925 was 2.5 per cent; in 1929, 1.8 per cent. In 1929, 700 women applied to the commission for aid; 1,227 women were confined in the clinics or at home; there were 600 women concerning whom no information was furnished. The plan of the commission is as follows: (1) direct social and medical aid comprising medical services of the commune, physicians of the commune, and midwife institutions for patients; (2) information and aid furnished pregnant women by the communal authorities, by the public, by the police and through a consultation bureau for pregnant mothers on the care of infants; (3) aid for mothers and for the child (before, during and after birth), and (4) giving out of available aid funds.

Exhibit on "Mother and Child"

Under the chairmanship of Prof. A. H. M. J. Van Rooy, a permanent committee has been appointed whose duty it will be to prepare an exhibit devoted to "mother and child." This exhibit, patterned after similar exhibits in foreign countries, will illustrate in as instructive and complete a manner as possible all that concerns the relations of "mother and child." The purpose is to serve the interests of the people—interests of paramount importance, and to bring to all classes of society the best ideas on hygiene, in order to combat false ideas and to bring about a restoration of the strength of the people in general, and, more particularly, of the public health.

Congress on Aid to Invalids

The first Congress on Aid to Invalids was held in Geneva, two years ago. Representatives of the United States, Canada and eleven of the principal countries of Europe, the Netherlands among the number, took part in the second congress, which was held recently at The Hague. Four points were proposed: (1) the constant and prompt ferreting out of all invalids; (2) the application of suitable medical and surgical treatment; (3) special instruction, when necessary, to provide a means of livelihood, and (4) the securing of employment suitable for the invalid. Such was the program of the Netherlands; what other countries thought about it was possible through the holding of international conventions. However, account must be taken of the economic situation of each country. Also the collaboration of the central government is needed.

Another question is whether special orthopedic hospitals are needed or whether an orthopedic service should be established in every hospital. According to Dr. Brocx, that would be the solution for the large hospitals; for those of less importance it would be desirable to add an orthopedist to the staff.

Professor Hofman of Frankfort-on-Main spoke on "The Future of Orthopedics." Mrs. E. Reeves Solenberge spoke on "Some Agencies and Institutions for Cripples, in Various European Countries."

Marriages

BRADFORD MASSEY, Berlin, Md., to Miss Sarah D. Snook of Lewistown, Pa., in New York, March 5.

WILLIAM JOHN RYNEARSON, Fenton, Mich., to Miss Alberta Trollman of Tyrone, February 1.

HAROLD NUGEN, Auburn, Ind., to Miss Marian Kinch of Kalamazoo, Mich., February 20.

SAM HARRY ROSS, JR., Seneca, S. C., to Miss Edna Aileen Tollison of Greenville, March 5.

GLEN WALKER to Miss Fleta Clark, both of Herrick, Ill., in Covington, Ind., Nov. 12, 1931.

EDWARD H. BARKSDALE, Nashville, Tenn., to Miss Louise Paty of Bell Buckle, March 5.

GERALD G. CLEARY, San Francisco, to Miss Berenice Campbell of Chicago, Dec 12, 1931.

MARCEL S. BROWN, Spencer, Ind., to Miss Margaret Maple of Sullivan, February 14.

JOHN BERTRAM FITZGERALD to Miss Mildred Guinn, both of Chicago, February 3.

ISADORE MALLIN to Miss Emma Adeline Polin, both of Chicago, February 2.

Deaths

James Birney Guthrie ✠ New Orleans; Tulane University of Louisiana Medical Department, New Orleans, 1900; professor of the principles and practice of medicine, Louisiana State University Medical Center; instructor in medicine, 1900-1906, assistant professor of medicine, 1906-1912, and professor of clinical medicine, 1912-1930, at his alma mater; fellow of the American College of Physicians; served during the World War; aged 56; senior visiting physician to Hotel Dieu Hospital and the State Charity Hospital; consultant in medicine, Touro Infirmary, where he died, March 8, of heart disease.

James Hendrie Lloyd, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1878; member of the Medical Society of the State of Pennsylvania; emeritus professor of neurology, University of Pennsylvania Graduate School of Medicine; for many years on the staffs of the Philadelphia General Hospital and the Methodist Episcopal Hospital; aged 78; died, March 14, of pneumonia.

Howard Hill ✠ Kansas City, Mo.; Kansas City Medical College, 1895; member of the Western Surgical Association and the American Association of Anatomists; fellow of the American College of Surgeons; surgeon to St. Joseph's Hospital and visiting surgeon to Kansas City General Hospital; aged 63; died, February 24, of angina pectoris.

William John Rothwell, Murray, Utah; Jefferson Medical College of Philadelphia, 1873; member of the Colorado State Medical Society; emeritus professor of medicine, University of Colorado School of Medicine, Denver; formerly on the staffs of the Jewish Hospital for Consumptives and St. Anthony's Hospital, Denver; aged 92; died, February 14.

Charles Sixtus Rehfeldt ✠ St. Louis; Missouri Medical College, St. Louis, 1896; formerly professor of physical diagnosis, National University of Arts and Sciences Medical Department; served during the World War; aged 58; died, February 13, of cerebral thrombosis, angina pectoris and chronic myocarditis.

John Nelson Warren, Los Angeles; Miami Medical College, Cincinnati, 1871; fellow of the American College of Surgeons; formerly professor of principles and practice of surgery and clinical surgery, Sioux City (Iowa) College of Medicine; aged 85; died, February 20, in the Hollywood Hospital, of senility.

George W. Stoner ✠ Senior Surgeon, U. S. Public Health Service, retired, Staten Island, N. Y.; Bellevue Hospital Medical College, New York, 1876; Jefferson Medical College of Philadelphia, 1881; aged 78; died, February 7, in the U. S. Marine Hospital, Baltimore, of cerebral hemorrhage.

Arthur MacNeal ✠ Berwyn, Ill.; Rush Medical College, Chicago, 1892; aged 64; medical director and superintendent of the Berwyn Hospital, where he died, March 13, of septicemia and pyemia following a slight punctured wound of the hand received while treating a patient.

William Bryan ✠ Staten Island, N. Y.; University of the City of New York Medical Department, 1880; fellow of the American College of Surgeons; on the staffs of the Staten Island Hospital and St. Vincent's Hospital; aged 71; died, February 25, of heart disease.

George Hildreth Camp, Freedom, Pa.; George Washington University Medical School, Washington, D. C., 1905; member of the Medical Society of the State of Pennsylvania; aged 61; died, February 17, in Rochester, of chronic myocarditis and arteriosclerosis.

James Madison Morris, Lexington, Ky.; Tennessee Medical College, Knoxville, 1902; served during the Spanish-American and World wars; medical director of the Kentucky House of Reform, Greendale; aged 58; died, February 12, of heart disease.

Walter Lowry Henderson, East McKeesport, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1902; member of the Medical Society of the State of Pennsylvania; served during the World War; aged 55; died, February 18, of pneumonia.

Edmund Boleslaus Dywinski, Buffalo; University of Buffalo School of Medicine, 1923; member of the Medical Society of the State of New York; aged 34; died, January 30, in the J. N. Adam Hospital, Perrysburg, of pulmonary tuberculosis.

William Westbrook Redfern, Coldwater, Mich.; Graduate School of Medicine of the Division of Biological Sciences of the University of Chicago, 1930; physician to the State Public School; aged 33; died, February 7, of bronchopneumonia.

Howard Drumm, Muncie, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; member of the Indiana State Medical Association; aged 56; died, February 22, in the Ball Memorial Hospital, of pneumonia.

Charles James McGee ✠ Leavenworth, Kan.; University Medical College of Kansas City, 1902; fellow of the American College of Surgeons; visiting surgeon to St. John's and Cushing hospitals; aged 55; died, February 29, of a skull fracture.

Frederick G. Watson, Worthington, Minn.; Medical Department of Hamline University, Minneapolis, 1903; member of the Minnesota State Medical Association; aged 60; died, January 11, of coronary thrombosis and cardiac decompensation.

Chester Winfred Smith, Glendora, Miss.; Memphis (Tenn.) Hospital Medical College, 1906; member of the Mississippi State Medical Association; aged 72; died, February 22, in the Baptist Hospital, Memphis, of aneurysm of the aorta.

William Louis Miller, Wadesville, Ind.; Medical College of Indiana, Indianapolis, 1901; member of the Indiana State Medical Association; aged 58; died, January 28, in Evansville, of hepatitis, duodenal ulcer and cholecystitis.

Jacob G. Lawrence, Canton, Ohio; Western Reserve University Medical Department, Cleveland, 1897; member of the Ohio State Medical Association; aged 65; died, February 17, in the Aultman Hospital, of heart disease.

Harry Lavinton Purdy ✠ New York; College of Physicians and Surgeons in the City of New York, 1890; aged 64; died, February 26, in the Fifth Avenue Hospital, of general peritonitis following acute diverticulitis.

Zebian Headley Weyant, Kansas City, Mo.; University Medical College of Kansas City, 1898; veteran of the Spanish-American War; formerly a druggist; aged 59; died, January 29, of chronic fibrous myocarditis.

James B. Kirkpatrick, Indianapolis; Medical College of Ohio, Cincinnati, 1879; for many years mayor of Kokomo, Ind., and member of the school board; aged 76; died, February 18, of mitral stenosis and pneumonia.

Frank Moore Burns, Cincinnati; Medical College of Ohio, Cincinnati, 1900; member of the Ohio State Medical Association; served during the World War; aged 57; died, February 29, of cerebral arteriosclerosis.

Michael O. Dumas, Washington, D. C.; Howard University School of Medicine, Washington, 1895; member of the board of trustees at his alma mater; aged 64; died, February 17, of chronic interstitial nephritis.

Norman Walter Connaway, Newark, Ill.; St. Louis College of Physicians and Surgeons, 1906; aged 60; died, February 25, in the Copley Hospital, Aurora, of injuries received in an automobile accident.

Talbert W. Blakeslee, Erie, Pa.; Eclectic Medical College of Pennsylvania, Philadelphia, 1879; Louisville (Ky.) Medical College, 1899; aged 71; died, February 3, of uremia and cerebral hemorrhage.

William Finley Moss ✠ Maineville, Ohio; Starling Medical College, Columbus, 1882; Jefferson Medical College of Philadelphia, 1891; aged 76; died, February 24, of arteriosclerosis and myocarditis.

Hal Wyman Hogue ✠ Montpelier, Ohio; Northwestern University Medical School, Chicago, 1913; member of the West Virginia State Medical Association; aged 42; died, February 19, of pneumonia.

Hawkins Whitworth Corbett ✠ Anderson, S. C.; North Carolina Medical College, Charlotte, 1914; president of the Anderson County Medical Association; aged 42; died, February 27, of pneumonia.

Robert Ernest Blackerby, Tollerburg, Colo.; Barnes Medical College, St. Louis, 1899; member of the Colorado State Medical Society; aged 59; died, February 5, of a self-inflicted bullet wound.

George Omer Lavallee ✠ Lowell, Mass.; Harvard University Medical School, Boston, 1896; on the staff of the Lowell Tuberculosis Hospital; aged 58; died, January 12, of endocarditis and sinusitis.

Henry F. Bruning ✠ Chicago; Medical College of Virginia, Richmond, 1891; on the staffs of the Alexian Brothers Hospital and the Grant Hospital; aged 60; died, March 8, of lobar pneumonia.

Edwin Allen Martin, South Bend, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; formerly county coroner; aged 59; died, February 13, of heart disease.

Andrew Bascome Nichols, St. Louis; Missouri Medical College, St. Louis, 1873; aged 79; died, January 29, in the Missouri Baptist Hospital, of carcinoma of the prostate and acute myocarditis.

Claude Malvern Kelton, Clark, Colo. (licensed, Tennessee, 1908); member of the Tennessee State Medical Association; veteran of the Spanish-American War; aged 55; died, in February, of asthma.

William Quail Skilling ✠ Lonaconing, Md.; University of Maryland School of Medicine, Baltimore, 1883; aged 72; died, February 6, in the Union Memorial Hospital, Baltimore, of pneumonia.

William Carman Allison, Kalispell, Mont.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1913; aged 39; died, January 14, of influenza, pneumonia and embolism.

Robert Curtis Brown ✠ Milwaukee; College of Physicians and Surgeons in the City of New York, 1892; served during the World War; aged 64; died, February 26, of coronary occlusion.

Charles Miller Hatcher ✠ A. Surg. Lieut., U. S. Navy, retired, Presidio, Texas; Medical College of Virginia, Richmond, 1917; aged 43; died, Dec. 27, 1931, of pulmonary tuberculosis.

James Chapple, Billings, Mont.; Trinity Medical College, Toronto, Ont., Canada, 1900; member of the Medical Association of Montana; aged 61; died, January 30, of heart disease.

Lorenzo Norton, East Baldwin, Maine; Bellevue Hospital Medical College, New York, 1883; aged 74; died, January 29, in Cornish, of carcinoma of the prostate gland and rectum.

Elwood Robison, Glendale, Calif.; University of Indianapolis Medical Department, 1902; aged 56; died, January 20, of chronic myocarditis and acute dilatation of the heart.

Truman E. Fairall, Tecumseh, Neb.; University of Maryland School of Medicine, Baltimore, 1873; aged 80; died, January 31, of a fractured hip received in a fall.

John James Cameron, Kearney, Neb.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1888; aged 67; died suddenly, February 20, of angina pectoris.

Robert Calhoun Caldwell, Bradley, Okla.; University of Louisiana Medical Department, New Orleans, 1876; aged 80; died in Fort Worth, January 21, of senility.

Helen Louise Smith, Takoma Park, Md.; University of Michigan Medical School, Ann Arbor, 1891; aged 69; died suddenly, January 21, of heart disease.

Edwin Valentine Heaton, Lynnville, Ill.; Barnes Medical College, St. Louis, 1896; aged 61; died, February 6, in Jacksonville, of a self inflicted bullet wound.

William Faurman Turner, East St. Louis, Ill.; American Medical College, St. Louis, 1897; aged 73; died, January 28, in the Christian Welfare Hospital.

Benjamin F. Hamilton, Shawnee, Okla.; Medical College of Ohio, Cincinnati, 1884; aged 74; died, February 12, of nephritis and mitral regurgitation.

James Leroy Cummins, Anderson, Ind.; Curtis Physio-Medical Institute, Marion, 1889; aged 75; died, February 11, of hemorrhage of the stomach.

George E. Baudry, Atchison, Kan.; Hahnemann Medical College and Hospital, Chicago, 1892; aged 66; died, January 23, of general peritonitis.

James Newton Alexander, Roundup, Mont.; Jefferson Medical College of Philadelphia, 1894; aged 59; died, January 23, of cerebral hemorrhage.

Patrick H. Stafford, Grapeland, Texas; Barnes Medical College, St. Louis, 1905; aged 53; died, January 31, of pneumonia, following influenza.

John D. Ward, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1887; aged 66; died, February 5, of chronic myocarditis.

Joseph A. Kerschner, Lithopolis, Ohio; Ohio Medical University, Columbus, 1906; aged 59; died, February 3, of cerebral hemorrhage.

E. C. Perkins, Alma, Ga.; University of Georgia Medical Department, Augusta, 1902; aged 54; died, January 19, of myocarditis.

Henry Stout Pettit, Brooklyn; Long Island College Hospital, Brooklyn, 1890; aged 65; died, February 8, of heart disease.

John W. Scott, Springfield, Ill.; Chicago Medical College, 1876; aged 76; died, Dec. 12, 1931, of general debility.

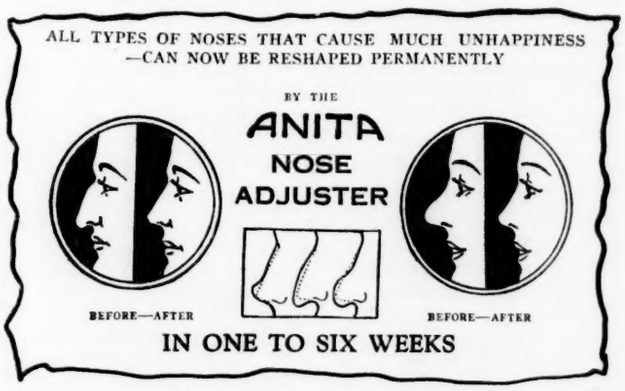
Samuel T. Songer, Ashland, Ore.; Medical College of Ohio, Cincinnati, 1871; aged 94; died, Dec. 25, 1931.

Bureau of Investigation

THE ANITA NOSE ADJUSTER AND DR. JOSEPHS NOSE CORRECTOR

Two Concerns Debarred from the Mails by Postal Fraud Orders

On February 17, 1932, the Post Office Department issued a fraud order against the Anita Institute, Inc., of Newark, N. J., and Dr. Josephs, Inc., of East Orange, N. J. Both of these concerns, according to a report recently issued by the United States postal authorities, are run by the same people and both of them sell alleged nose shapers. The Anita Institute was started in 1913 by Mrs. Anna D. Rostow; it was incorporated in 1923. Mrs. Rostow is president and treasurer; Herman Rice, vice president; Joseph Ross, secretary, and Lawrence Rostow, office manager. The same persons are officers of Dr. Josephs, Inc., which came into existence in 1929. The Anita Institute's device was advertised as the "Anita Nose Adjuster"; the Dr. Josephs concern's device was called "Dr. Josephs Nose Corrector." The devices were essentially identical. For some years, the Anita Institute has been advertising its "adjuster" and claiming, either directly or by implication, that the shape of the adult nose could be changed by wearing it. The public might be led to believe that a snub nose could be changed into a Grecian, or a retroussé into a Roman.



In the June, 1930, number of *Hygeia,* in the "Questions and Answers" department, there was a question asked relative to "nose adjusters," and the answer published read in part: "There is no device that will change the shape of the adult nose. Devices sold for that purpose are shrewd schemes for getting money out of persons who are worried about the shape of the nose." Soon after the appearance of that issue of *Hygeia,* a letter came from the Anita Institute, signed by Mrs. A. D. Rostow, president, and quoting that part of the answer that has just been given. Mrs. Rostow then stated:

"We call to your attention that this statement is a direct libel against our appliance, the Anita Nose Adjuster, which can and does correct fleshy and cartilaginous malformations of the adult nose. . . . We therefore request that in full fairness a retraction be made in your next issue."

As the statement in *Hygeia* was considered scientifically sound, no retraction was made.

According to the advertising put out by the Anita Institute, "until the Anita Nose Adjuster was invented, it was necessary to resort to expensive and painful plastic operations, in order to overcome nasal deformities. Now this is all changed." Some other claims made were:

"A perfect nose in one to six weeks."

"No matter how irregular the fleshy contour of the nose, the Anita Nose Adjuster will make it beautifully straight and normal—in from one to six weeks."

"Although no two noses are exactly alike in shape and size, bear in mind that the Anita is the world's ONLY nose corrector that fits every case like a glove."

In December, 1930, the Anita Institute, through its president, Mrs. Rostow, submitted to the Bureau of Investigation of the American Medical Association what purported to be evidence for the claims made for her device. Part of this evidence con-

sisted in the submission of several copies of a questionnaire of three questions which were alleged to have been answered by physicians, and to have been based on the knowledge of such physicians of the Anita Nose Adjuster. The first and essential question in the questionnaire was: "In your opinion, can flesh and cartilage be reshaped?" To this, certain physicians had answered "Yes." In order to check on this material, the Bureau of Investigation wrote to six of the physicians whose names were signed to the questionnaire and asked whether they had answered the question already quoted in the affirmative, as stated. The Bureau of Investigation pointed out that the question itself was vague, because no distinction was made between the nose of a child and the nose of an adult, nor was anything said as to whether operative procedures had been performed prior to the alleged reshaping. The physicians were therefore asked whether, in their reply, they had reference to the nose of an adult or that of a growing child, and they were also asked what their answers would have been had the question been propounded as follows:

"In your opinion, can the shape of an adult nose be changed without operation and by the simple wearing of a device applied externally?"

Five of the six physicians who were written to replied, and in every instance these physicians stated unqualifiedly that, in their opinion, the shape of an adult nose could *not* be changed by the simple wearing of a device applied externally! One of the five physicians—Dr. Harry A. Brotman of Newark, N. J.—nine months afterwards, wrote to the Bureau of Investigation and stated that while he had definitely said that the shape of an adult nose could not be changed without an operation by the simple wearing of a device applied externally, now stated that he was of the opinion that if the "question had been limited to the fleshy and cartilaginous portions of the nose," his answer would have been "Yes"! In other words, Dr. Brotman seems to go on record as taking the attitude that the fleshy and cartilaginous portions of an adult nose *can* be changed by the wearing of an Anita Nose Adjuster.

In the memorandum that the Hon. Horace J. Donnelly, Solicitor of the Post Office Department, sent to the Postmaster General when he recommended the issuance of a fraud order in this case, it was brought out that expert testimony on behalf of the government showed that the only manner in which the shape of an adult nose can be permanently changed is by surgical interference, and that Mrs. Rostow's theory as to the alleged ability of her device to force the permanent migration of nasal tissue in the adult to more desirable positions, is contrary to scientific teaching. Judge Donnelly also brought out that evidence was introduced at the hearing to show that the Anita Nose Adjuster would not re-form the noses of adult persons which are hooked, pointed, snub or drooping.

Incidentally, the memorandum stated that Lawrence Rostow, son of Mrs. Rostow and office manager of the Anita Institute, was present at the hearing in Washington, and that he "has himself a nose bent laterally." Mrs. Rostow was asked why her device was not used to correct this abnormality and she stated that her son had been unable to wear the appliance for a sufficient length of time "on account of his ears being in the way." This reminds one of the classic joke of the small boy whose only objection to watermelon was that "it muses up your ears."

The government also brought out the fact that while some of the pictures shown in the Anita Institute literature included the type of nose common to the Negro race, Mrs. Rostow admitted at the hearing that her device would not change the nasal organ of the Negro to the Caucasian type. In the memorandum, Judge Donnelly, in discussing the claims made by Mrs. Rostow for her device, that "doctors approve it," stated:

"While some favorable comment with respect to these appliances appears to have been secured by the promoters thereof from few reputable physicians, the evidence shows that in a number of instances such comment has been obtained as a result of a questionnaire framed in a misleading manner and which made no distinction between the child and adult nose. Several of the physicians involved in this connection, upon being apprised of all the facts in the matter, repudiated their former statements."

The Anita Institute advertising has always emphasized the money-back refund guarantee. This read as follows:

"We guarantee to refund your money, if after thirty days' use you have not benefited by the ANITA NOSE ADUSTER, provided you have used it regularly and it is returned to us by registered mail."

Of this feature the Solicitor's memorandum states: "The evidence shows that it is the consistent policy of the promoters thereof to avoid living up to their promise in that respect whenever possible."

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

USE OF CASTOR OIL AND QUININE DURING LABOR

To the Editor:—I recently attended the birth of a nine pound still-born baby. An ounce of castor oil and 30 grains of quinine sulphate were given the prospective mother one month previously and also thirty-six hours previously. The quinine sulphate was given in three doses of 10 grains two hours apart. What is the probability of the quinine sulphate having caused the infant's death? There was a slight maceration of the skin, and the umbilical cord had a green discoloration. How soon after intra-uterine death would these changes start? The child was one week past due. Please omit name.

M.D., Wisconsin.

ANSWER.—Most nine pound babies are somewhat postmature and the mortality is higher for postmature babies than for babies that are born at term. The higher death rate is due to the longer and harder labors and the more frequent necessity for operative intervention. In a few instances, overterm babies die in utero without any apparent cause. Even a necropsy may fail to reveal the cause of death in these cases. There is small likelihood that the 2 Gm. (30 grains) of quinine caused the death of the child in this case. The quinine administered one month before delivery certainly had no deleterious effect. There are a few case reports in the literature (Gellhorn, Torland, McSwiney, Dilling and Gemmell, De Lee and Greenhill) wherein children died after the administration of quinine to induce labor and no explanation other than the quinine could account for the death of these children. There is experimental evidence to prove that quinine may produce intra-uterine fetal death, but the statistics of Sadler, Dilling and Gemmell show that this risk is not greater than that of stillbirths from undiscoverable causes in otherwise normal labors. Postmortem examination on many children born dead after the use of quinine show intracranial injuries. This suggests that there is a mechanical difficulty in delivery in many of these cases. The presence of meconium in the liquor amnii is more frequent after quinine, and intra-uterine asphyxia is the probable cause of this. There is no evidence to show that quinine is a stimulant to fetal intestinal muscle.

Intra-uterine changes in fetuses are not constant because many factors are involved, such as rupture of the membranes, intra-uterine infection and the age of the fetus at the time of death. A green discoloration of the umbilical cord may occur a few hours after meconium has been passed into the liquor amnii. Maceration of the skin may be noted a few hours after death, but it is usually not observed until a fetus has been dead a few days. It would be of importance to know when the patient felt the baby move for the last time and also when the fetal heart tones were last heard in this case.

HYPERPLASTIC HYALINE PERISPLENITIS

To the Editor:—Please give prognosis in a case of tuberculous spleen ("frosted spleen") as to life expectancy and as to ultimate recovery, with ability to make a living. Splenectomy was done. Please omit name.

M.D., Michigan.

ANSWER.—Frosted spleen is another term for hyperplastic hyaline perisplenitis. This condition may be secondary to any sort of inflammatory process involving the capsule of the spleen and is not ordinarily tuberculous in nature, although it may be associated with tuberculosis. Tuberculous splenitis probably never occurs as a primary condition; it usually has been preceded by some other focus in the body. Tuberculosis of the spleen has been observed as a coincidental condition in conjunction with hemorrhagic purpura, leukemia, hemolytic icterus, polycythemia, and splenic anemia.

A few cases of splenectomy have been reported for what seems to have been considered primary tuberculosis of the spleen.

Following splenectomy for so-called primary tuberculosis, satisfactory recovery has been reported in two thirds of the cases, and some of the patients are living twelve and fourteen years after splenectomy. Not infrequently, tuberculosis becomes active elsewhere in the body following splenectomy, and either pulmonary tuberculosis or widespread miliary tuberculosis has developed. Therefore, in the individual case it is impossible to give a satisfactory prognosis as to ultimate recovery or life expectancy; prognosis depends chiefly on the patient's general resistance to tuberculosis.

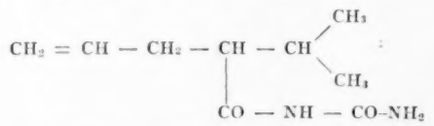
THE USE OF BARBITAL COMPOUNDS

To the Editor:—I was deeply interested in the splendid article on the intravenous use of barbital compounds. One of the most grave faults in the training of medical students in most of the schools is the scant attention paid to the teaching of prescription writing and applied therapeutics. This I have briefly expressed in the enclosed review. As one of the chiefs of the Philadelphia General Hospital, I come in contact with interns from all parts of the country and find not only that in general they lack the training in prescribing but that they do not forsee the dangers confronting the public by their more or less unconscious resort to proprietaries about which they know nothing. Some time ago, a wave of enthusiasm passed over my interns when they gave members of the barbital group intravenously. This I promptly stopped in my own service. On two occasions recently I have seen mental excitation follow the administration of "Sedormid" by mouth, and it is about this that I seek your advice. This is said to be "allylisopropylacetylcarbamide." Carbamate, I believe, is an intermediate product in the formation of urea and is, I understand, quite toxic. Whether a carbamide may be similarly toxic, and more so when a liver is already damaged, I do not know. One of the two patients has been an intermittent fibrillator for two years at least and must have an appreciable degree of damage in the liver. The other has a multiple infectious arthritis and, from the offensive character of the stools, probably a high bacterial content. Four blood cultures have been negative. He has had an intermittent fever for a period of seventeen weeks, and when I saw him recently I learned that he had been given "Sedormid" and cinchophen. He has a slight enlargement of the liver and doubtless some parenchymatous degeneration. Both of these patients improved after the attempt at sedation was stopped. Will you enlighten me as to the structural relationship between carbamides and carbamates? Are both toxic, and is it possible that my assumption is correct? Are the barbital members eliminated more or less completely as urea? This claim is made especially for the di-allyl-malonyl-urea member. If so, do they pass through the carbamide or carbamate state? If they do, then it is perfectly conceivable that a definitely damaged liver would interpose a potently dangerous factor in the administration of this group.

WILLIAM E. ROBERTSON, M.D., Philadelphia.

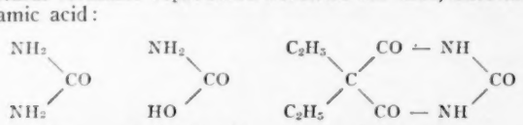
ANSWER.—The Council on Pharmacy and Chemistry has not accepted "Sedormid" for inclusion in New and Nonofficial Remedies, nor has the firm requested consideration of the product.

"Sedormid" is a carbamide—chemically, allyl-isopropyl-acetyl-carbamide, having the structural formula:



It may be looked on as a chemical decomposition substance of allyl-isopropyl-malonylurea (allyl-isopropyl barbituric acid), which is the hypnotic component in the nonaccepted but widely advertised proprietary "Allonal."

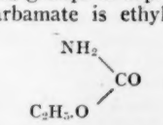
The relationship of these substances may be illustrated by the structural formulas reproduced herewith for urea, barbital, and carbamic acid:



Urea Carbamic acid Barbital

Carbamide is another name for urea. The chief difference between carbamic acid and carbamide is that, in the case of the former, one of the NH_2 groups is replaced by an HO.

The best known carbamate is ethyl carbamate (urethane):



The occurrence of mental excitation is a common sequel to hypnotic medication. It is commonly reported after the barbitals and bromides. Therefore, it is not surprising that it has occurred after the administration of "Sedormid." It is conceivable that certain disease conditions which would promote accumulation of the drug in the body would favor the occurrence of mental excitation. This aspect of hypnotic medication with "Sedormid" is not referred to in the manufacturer's literature, which gives the impression that the drug is safe and gently acting.

It is conceivable that a damaged liver could contribute to manifestations of toxicity from "Sedormid." The liver is probably the seat for destruction of drugs in general, including the group of hypnotics. Experimentally, ethyl carbamate is known to cause vacuolar degeneration of the liver, a phenomenon that has been reported for other hypnotics. Although the effects of "Sedormid" on the liver have not been investigated, and the drug is chemically different from the carbamates, the probability of hepatic action similar to that of the carbamates should be kept in mind.

The pharmacologic actions of "Sedormid" have been studied only to a limited extent. A paper by Demole (*Deutsche med. Wchnschr.* **54**:1166, 1928) contains a summary report of its effects on the circulation, respiration and urinary excretion. However, the report lacks essential data and details which would enable a satisfactory assessment of the value of the results claimed. Demole asserts that circulatory depression in dogs was absent during narcosis from "Sedormid" but he does not show any details or records of the changes. In rabbits, which were insensitive to "Sedormid," the blood pressure was not affected, but rodents are generally less sensitive to hypnotics than other mammals, especially man. The fall of body temperature was marked and well sustained. It was surprising that the respiration was so markedly depressed in view of the claimed absence of circulatory depression. These changes do not harmonize, and the chemical composition of "Sedormid" scarcely suggests an exclusive or specific respiratory depression. If a general medullary depression occurs after "Sedormid," as is entirely possible, depression of the vasomotor system would occur and this might be more marked in circulatory disorders. Demole indicates nothing of possible cardiac actions from concentrations of "Sedormid" within the therapeutic range, but depression is frequently demonstrable with hypnotics. Demole studied the urinary excretion in one dog and reports considerable oxidation of "Sedormid," but the urine contained something with the melting point of "Sedormid," although the method of quantitative estimation and tests for identification of "Sedormid," other than the melting point, are not given. From these scanty data, it is suggested that "Sedormid" may occur as such in the body and that it may be quite depressing for the higher functions. If this is true, the drug should be used cautiously, if at all, in patients with cardiac disorders, such as fibrillation, and with liver disease. From the fact that the correspondent's patients improved after the use of the "Sedormid" was stopped, it is suggestive, though not conclusive, that some relationship existed between the liver and cardiac conditions and the actions of the drug. However, it must be kept in mind that improvements in these conditions could occur as the result of rest alone.

Pharmacologically, it is known that hypnotics and analgesics, or antipyretics, can increase one another's actions. Therefore it is conceivable that "Sedormid" could increase the toxic action of cinchophen on the liver; likewise, cinchophen could increase the hypnotic action of "Sedormid." However, the actions of these two drugs on each other have not been investigated. The existence of these possibilities, together with the unexplained peculiar actions of "Sedormid" on the higher functions, and the comparative absence of data on pharmacologic actions in general, merely indicate the undesirability of premature exploitation of this new hypnotic. Incidentally, the clinical reports on "Sedormid" are too vague and incomplete, being in the nature of testimonials embodying impressions and opinions, to warrant the claim that "Sedormid" is superior to other hypnotics and comparatively safe.

The barbitals are eliminated for the most part as such; destruction occurs to the extent of about 30 to 40 per cent. Amytal is claimed to be completely destroyed. The excretion is rather variable, depending on diuresis and perhaps on other functions and organs not yet sufficiently evaluated. In view of the possibility that the chemical changes in the barbitals occur in the liver, the existence of liver damage would tend to increase the bodily accumulation of undestroyed barbitals. Until evidence appears to the contrary, it is safer to consider the existence of hepatic disease as a contraindication to the free or continued use of barbitals, and to other hypnotics as well. In fact, a warning to this effect has already been given by Trémolières, Tardieu and Carteaud (*Bull. Acad. de méd.* **100**:1459, 1929). These authors based their opinion on the discovery of hepatic degeneration, manifested by cloudy swelling and vacuolization and fatty changes in livers of suicidal poisoning from diallylbarbituric acid and diallylmalonylurea, and on experimental confirmation of these hepatic changes in rabbits receiving the last mentioned barbital compound.

DETACHMENT OF RETINA

To the Editor:—Could you give me the generally accepted ideas as to the cause of simple detachment of the retina? Have there been any thorough clinical investigations relative to the etiologic factors? What are the modern accepted opinions about this condition? A man, aged 21, has a retinal detachment of both eyes, situated in the lower quadrant in the right eye and the left lower quadrant in the left eye.

J. H. SCHRANT, M.D., Hutchinson, Kan.

ANSWER.—From the clinical point of view, detachment of the retina has been classed etiologically as traumatic, myopic, exudative, in pregnancy, and cryptogenic. In view of the more modern investigations, many theories as to the cause of detachment have been advanced, none of which have as yet been proved or accepted by others than the authors and their immediate schools. The following theories now have the most violent adherents:

1. Exudative processes of the choroid with serous exudation into the subretinal space with resultant mechanical elevation of the retina.

2. Transudative processes into the subretinal space by plasma from the choroidal plexus without active lesions of the choroid, such as in the detachments that occur in complicated pregnancies.

3. Formation of a hole in the retina by rarefaction of a Blessig vacuole, or by mechanical trauma, or by autolysis, with subsequent passage of vitreous into the subretinal space and resultant mechanical detachment. This is at present the favorite theory and is being played with all possible (as well as impossible) variations, mostly hypothetic.

4. Mechanical traction on the retina by vitreous strands.

DERMATITIS IN PORCELAIN WORKERS

To the Editor:—In an industrial plant that does a large amount of porcelain baking, I have come in contact with several cases of porcelain poisoning which do not respond to any treatment I have tried. I should appreciate it if you would tell me the solvent that is used and what in the contents of porcelain would cause a hyperemic weeping dermatitis to develop. Please omit name.

M.D., Michigan.

ANSWER.—No conclusive answer can be made to this query, owing to differences in practice from plant to plant, and owing to experimental work continually under way. Four possible causes of dermatitis among procelain workers may be enumerated:

1. Lime used in the glaze readily rubs off on the hands and forearms, and as a dust may settle on any exposed portion of the body.

2. Chrome salts used in the coloring of some porcelains may readily produce a dermatitis.

3. The mechanical action of chemically inert dusts settled on the skin, plus the action of excessive heat from the ovens, is a known source of dermatoses.

4. The detergents employed at the end of the workday may be so harsh as to induce skin lesions. The hazard of lead in this industry has prompted the practice of thorough cleansing of the person on leaving the work point, and paved the way for the use of irritant soaps.

Complication of a dermatitis caused by any of the aforementioned hazards by a secondary entry of fungi is always possible. This industry is known as one in which the products in process are handled by several persons with little intervening time. The transmission of ringworm and other communicable skin diseases is favored thereby.

TUBERCULOSIS AND PREGNANCY

To the Editor:—I have a patient with an arrested pulmonary tuberculosis of three years' duration. No other organic lesion is present. She is pregnant and anxious to carry on her pregnancy. Will you please tell me what is the best plan of procedure to prevent a rekindling of the old pulmonary lesion? What is the prognosis for the mother, and what susceptibility has the child to pulmonary tuberculosis? Please omit name.

M.D., New York.

ANSWER.—Most women with arrested pulmonary tuberculosis may safely bear children, but they should be under the care of an internist throughout each gestation. It is important for the patient to observe the general rules of hygiene rather rigidly. She should have a well balanced diet with a relatively large amount of milk and vegetables, should have sufficient sleep and a period of rest during the day, and should be out in the sunshine as much as possible. Viosterol, especially during the winter months when there is little sunshine, is of benefit. Symptoms that are especially to be looked for are fever, persistent cough, night sweats, loss of weight instead of a gain, dyspnea and hemoptysis. Since the pulmonary condition has been in abeyance for three years, the patient will most likely continue with her pregnancy in a normal way without harm. The spontaneous onset of labor may be awaited, and during the first stage a policy of watchful expectancy should be followed just as with other patients. Sedatives should be given to secure as much rest as possible.

Unless the second stage promises to be short, it should be curtailed as much as possible by a low forceps operation, provided the fetal head has reached the perineum. Otherwise it is best to leave the patient alone. Inhalation anesthesia should be avoided whenever possible. Local infiltration anesthesia should be employed instead. If a general anesthetic is necessary, ethylene is probably the safest. The patient must be closely watched during the puerperium because occasionally there is a recurrence of pulmonary tuberculosis at this time.

The death rate for babies born of mothers with outspoken tuberculosis is not much greater than it is for children of healthy mothers. However, if all the miscarriages and deaths in infancy are counted, there is a mortality of about 60 per cent before the end of the first year. Hence there is a constitutional inferiority in a large proportion of babies born of mothers with active pulmonary tuberculosis. The question of whether tuberculosis is transmitted from the mother to the child in utero is still unsettled. Some authorities maintain that this practically never occurs, while others insist that it is not infrequent. There is no doubt that tuberculosis may be found in some placentas and in a few new-born fetuses. However, in most instances in which infants show evidence of tuberculosis they acquired it after birth. They are born with a low resistance and, unless they are brought up under exceptionally good hygienic surroundings, they may contract the disease. In the case cited, if no symptoms or signs of tuberculosis can be detected after delivery, the child may safely be placed at the breast. If unfavorable symptoms make their appearance, it is best to separate the child from the mother, for a short time at least, unless there are ample facilities for isolation in the patient's home.

TEAR GAS — CHLORACETOPHENONE

To the Editor:—The officials of the bank of this city are interested in equipping the bank with gas guns for protection. One question that came up was that the effect of the gas was only temporary and that exposure to the fumes would not cause any permanent injury. Two eye, ear and nose specialists informed me that they were not familiar with tear gas and would not venture an opinion. What is the effectiveness of tear gas and is there any injurious effect that it might have on any one exposed to the fumes of it?

INQUIRER.

ANSWER.—This reply deals solely with the toxicity of pure chloracetophenone, and not with lacrimatory substances in general. Of the action of this substance, Colonel Vedder (The Medical Aspects of Chemical Warfare, Baltimore, Williams & Wilkins Company, 1925) says:

"Men exposed to the action of chloracetophenone exhibit the following symptoms: irritation of the eyes, lacrimation and burning of the more tender portions of the skin. In some cases there is a tendency toward increased salivation and irritation of the throat. Following exposure there may be some discomfort, but this is of relatively short duration, except in the case of exposure to very high concentrations or to low concentrations for prolonged periods. In these latter cases it may require twenty-four hours for the eyes to feel normal again. Men exposed experimentally to high concentrations for short periods of time were unable to open their eyes for several minutes after exposure. In some instances a conjunctivitis was observed which lasted several hours.

"Chloracetophenone has comparatively little effect on the skin of either man or animals. When applied in excess to the human skin, there is a burning sensation, slight rubefaction, and sometimes small vesicles appear. This inflammation subsides in about seven days. In vapor form the inflammation produced is very mild and is usually quite unimportant, although in exceptionally sensitive individuals it may prove quite harassing. Chloracetophenone has no effect on the lungs of man in any concentration that will be met with in the field.

"Dogs exposed to the toxic action of chloracetophenone exhibit great excitement, irritation of the eyes, nose and throat, lacrimation, salivation, nasal discharge and dyspnea. Vomiting, trembling and twitching of the limbs may occur. Following exposure there is usually a decided corneal involvement varying from a slight opacity to ulceration and blindness; soreness of the throat and coughing. A few dogs that died showed congestion and edema of the lungs, a true membranous tracheitis, and decided corneal opacity. It is quite impossible that the concentrations used on these animals should be ever encountered in the field."

Recently, the use of tear gases in connection with mob gatherings has led to the complaint of subsequent conjunctivitis.

It is reasonable to believe that enough irritation of the eyes or the throat may be produced by tear gases to pave the way for secondary bacterial invasion, with ensuing pharyngitis and conjunctivitis on occasion. However, the use of these substances properly manipulated is not to be condemned; on the contrary, it is recognized that their judicious use may be salutary in the protection of life and property and the maintenance of law and order. Misuse of chloracetophenone may lead to accidents, as shown by W. D. McNally in THE JOURNAL, January 2, page 45.

EFFECTS OF GLYCERIN INTRAVENOUSLY

To the Editor:—Kindly answer the following questions: 1. Is glycerin an indifferent and harmless chemical substance for the human organism when introduced intravenously? 2. Is it sterile, or should it be sterilized for intravenous administration? If so, what is the best method of sterilizing without destroying it? 3. What would you consider a maximum safe intravenous dose for an average human being? 4. How would the human organism dispose of glycerin when administered intravenously? Please omit name.

M.D., New York.

ANSWER.—1. No. It lakes blood, even in low concentration, leading to hemolysis and hemoglobinuria.

2. As glycerin is almost ineffective against spore formers, it must be sterilized, which may be done at autoclave temperature for fifteen minutes.

3. Does not seem to be available.

4. Glycerin disappears rapidly from the blood. Some of it is eliminated in the urine. Some of it is transformed in the system into sugar and glycerin and may serve as a substitute for dextrose in metabolism. Thus it has been shown, by experiments on rats, to be capable of relieving insulin coma and convulsions. It is too hemolytic, however, to be seriously considered as a food for intravenous administration.

GONORRHEAL ENDOCERVICITIS

To the Editor:—In the treatment of subacute gonorrheal endocervicitis, how efficient are local applications of 20 per cent mercurochrome solution as compared with the other antiseptics? What is the present status of mercurochrome as an antiseptic agent in general? What are the evidences of cure of gonorrhea in a female? Please omit name.

M.D., Indiana.

ANSWER.—The comparative evaluation of antiseptics is exceedingly difficult. In pelvic conditions in women, mercurochrome-220 soluble probably finds its greatest field of usefulness when employed in 4 per cent solution in the vagina, preliminary to obstetric procedures. As a curative agent, employed in the treatment of gonorrhea of the female genitalia, silver nitrate and its derivatives are frequently given preference.

ETIOLOGY OF HEMORRHOIDS

To the Editor:—Is it possible for hemorrhoids to be caused in a normal rectum by the lifting of excessive weights? Is it possible for the increase in intra-abdominal pressure to cause an acute dilatation of the hemorrhoidal veins with thrombosis? Please omit name.

M.D., North Dakota.

ANSWER.—Hemorrhoids are caused by blood being dammed back into hemorrhoidal veins which have no valves to prevent back pressure; therefore lifting excessive weights over a period of time would tend to produce hemorrhoids. Sudden increase of intra-abdominal pressure is one of the common causes of thrombosis of the hemorrhoidal veins.

CARBON DIOXIDE FROM FLOWERS IN SICKROOM

To the Editor:—In Queries and Minor Notes (THE JOURNAL, Dec. 5, 1931, p. 1731) I saw the item concerning the evolution of carbon dioxide from flowers. The statements made therein are somewhat confused and contrary to well known facts of plant respiration.

It is a fact that living plants, whether growing in soil or in the form of cut flowers, continuously produce carbon dioxide which results from the metabolism (oxidation) of carbohydrates, acids and other organic constituents. This process goes on day and night. In the light there is superimposed on this oxidation process a photosynthetic one in which carbon dioxide is elaborated into carbohydrates. Moreover, the latter process occurs only within the green tissues. Therefore, during the day not only is all the carbon dioxide consumed within the plant but also an additional amount which enters by way of the stomas. In the dark the photosynthetic process ceases and the carbon dioxide formed in the metabolic process is evolved as stated by the hospital superintendent.

Quantitatively, this gaseous exchange has no influence on the atmosphere of a hospital room, as the oxygen intake or carbon dioxide output for twenty-four hours would not equal in volume one or two breaths of the patient. See Kostychev's Plant Respiration and Spoehr's Photosynthesis.

K. S. MARKLEY, Washington, D. C.
Associate Biochemist, Bureau of Plant Industry.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

AMERICAN BOARD FOR OPHTHALMIC EXAMINATIONS: New Orleans, May 9. Montreal, Sept. 19. Sec., Dr. William H. Wilder, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: The general, oral and clinical examination will be held in New Orleans, May 10. Sec., Dr. Paul Titus, 1015 Highland Building, Pittsburgh.

AMERICAN BOARD OF OTOLARYNGOLOGY: New Orleans, May 9. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

ARIZONA: Phoenix, April 5-6. Sec., Dr. B. M. Berger, 12 N. Central Ave., Phoenix.

ARKANSAS: *Basic Science.* Little Rock, May 2. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock. *Regular.* Little Rock, May 10-11. Sec., Dr. Sam J. Allbright, Searcy. *Eclectic.* Little Rock, May 10. Sec., Dr. Claude E. Laws, 803½ Garrison Ave., Fort Smith. *Homeopathic.* Little Rock, May 10. Sec., Dr. Allison A. Pringle, Eureka Springs.

COLORADO: Denver, April 6-9. Sec., Dr. Wm. Whitridge Williams, 422 State Office Bldg., Denver.

IDAHO: Boise, April 5. Comm. of Law Enforcement, Hon. Emmitt Pfost, Boise.

ILLINOIS: Chicago, April 12-14. Supt., Mr. Paul B. Johnson, Springfield.

MINNESOTA: *Basic Science.* Minneapolis, April 5-6. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Regular.* Minneapolis, April 19-21. Sec., Dr. E. J. Engberg, 524 Lowry Bldg., St. Paul.

MONTANA: Helena, April 5. Sec., Dr. S. A. Cooney, Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, May 3-4. Dir., Mrs. Clark Perkins, Lincoln.

NEVADA: Carson City, May 2-4. Sec., Dr. Edward E. Hamer, Carson City.

NEW MEXICO: Santa Fe, April 11. Sec., Dr. P. G. Cornish, Jr., 221 W. Central Ave., Albuquerque.

RHODE ISLAND: Providence, April 7-8. Dir., Dr. Lester A. Round, 319 State Office Building, Providence.

WISCONSIN: *Reciprocity.* Milwaukee, April 6. Sec., Dr. Robert E. Flynn, 315 State Bank Bldg., LaCrosse.

Illinois October Report

Mr. Paul B. Johnson, superintendent, Illinois Department of Registration and Education, reports the written and practical examination held at Chicago, Oct. 13-15, 1931. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Seventy-two candidates were examined, 66 of whom passed and 6 failed. Twenty physicians were licensed by reciprocity with other states and 6 physicians were licensed by endorsement from Nov. 24 to Dec. 21, 1931. The following colleges were represented:

PASSED

College	Year Grad.	Per Cent
Chicago Medical School	(1927) (1930) 77, (1931) 77, 78, 78, 78, 79	75,
Loyola University School of Medicine	(1929) (1930) 82, (1931) 77, 77, 78, 79, 80, 80, 81, 84	84,
Northwestern University Medical School	(1928) (1931) 79, 80, 81, 82, 84, 84, 86, 87	82,
Rush Medical College	(1931) 78, 79, 80, 80, 80, 81, 81, 81, 81, 82, 83, 83, 84, 86	78,
University of Illinois College of Medicine	(1931) 78, 78, 79, 79, 79, 80, 80, 81, 82, 85, 85, 86	76,
Indiana University School of Medicine	(1928) 79, (1929)	79
Johns Hopkins University School of Med.	(1924) 80, (1929)	79
Washington University School of Medicine	(1927)	80
University of Nebraska College of Medicine	(1928)	77, 78
Medical College of Virginia	(1930)	77*
University of Vienna Faculty of Medicine	(1925)†	81
University of Havana Faculty of Medicine and Phar.	(1927)	75
Charles University Faculty of Medicine, Prague	(1919)	76
German University of Prague Faculty of Medicine	(1921)	75*

FAILED

College	Year Grad.	Per Cent
Chicago Medical School	(1931)	72
Loyola University School of Medicine	(1930) 83,‡ (1931)	74, 81‡
Northwestern University Medical School	(1931)	78§
Rush Medical College	(1931)	74

LICENSED BY RECIPROCITY

College	Year Grad.	Reciprocity with
University of Arkansas School of Medicine	(1927)	Arkansas
Howard University School of Medicine	(1927)	W. Virginia
Northwestern University Medical School	(1929)	Minnesota
University of Illinois College of Medicine	(1931, 2)	Mississippi
State University of Iowa College of Med.	(1925), (1926)	Iowa
University of Kansas School of Medicine	(1920)	Kansas
University of Michigan Medical School	(1930)	Michigan
St. Louis University School of Medicine	(1921) (1930, 2)	Oregon, Missouri
Washington University School of Medicine	(1928) (1930, 2)	Colorado, Missouri
University of Pennsylvania School of Medicine	(1924) (1925)	Penna., Minnesota
Meharry Medical College	(1930)	Kansas, Tennessee
University of Vienna Faculty of Medicine	(1903)	Wisconsin

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Loyola University School of Medicine		(1930)	U. S. Navy
Northwestern University Medical School		(1931)	N. B. M. Ex.
Rush Medical College		(1931)	N. B. M. Ex.
Johns Hopkins University School of Medicine		(1928)	N. B. M. Ex.
Washington University School of Medicine		(1930)	N. B. M. Ex.
University of Pennsylvania School of Medicine		(1925)	N. B. M. Ex.

* Failed clinical test. Papers reviewed and given passing grade. Licenses recommended for issuance at February, 1932, meeting.

† Verification of graduation in process.

‡ Failed clinical test.

§ Failed in chemistry, physiology, pathology and bacteriology.

Ohio June Examination

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports the oral, written and practical examination held at Columbus, June 2-5, 1931. The examination covered 10 subjects and included 80 questions. An average of 75 per cent was required to pass. Two hundred and twenty-eight candidates were examined, 223 of whom passed and five failed. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine		(1930)	83.2, (1931) 84.5
Howard University School of Medicine		(1930)	75.5
Graduate School of Medicine of the Division of the Biological Sciences, University of Chicago		(1931)	83.5
Rush Medical College		(1929)	75.7, (1931, 2)*
Johns Hopkins University School of Medicine		(1926)	83.8
Harvard University Medical School		(1930)	83.1
St. Louis University School of Medicine		(1930)	80, 85.3, (1931) 82.5
University of Nebraska College of Med.		(1928)	80.4, (1929) 84
Cornell University Medical College		(1930)	79.6
New York Homeo. Med. College and Flower Hospital		(1931)	84
University of Rochester School of Medicine		(1930)	81.3, 84.7, (1931) 87.1
Ohio State University College of Medicine		(1931)	79.7, 79.8, 80, 80.5, 80.7, 80.9, 81.1, 81.4, 81.5, 81.5, 81.7, 81.8, 81.8, 81.8, 82, 82, 82.1, 82.3, 82.4, 82.8, 82.9, 83.1, 83.1, 83.3, 83.3, 83.3, 83.4, 83.5, 83.6, 83.6, 83.7, 83.7, 83.7, 83.8, 83.9, 84, 84, 84, 84.2, 84.3, 84.3, 84.4, 84.5, 84.8, 84.8, 84.9, 84.9, 85, 85, 85, 85, 85.1, 85.2, 85.6, 85.6, 85.9, 86, 86, 86, 86.1, 86.1, 86.2, 86.4, 86.4, 86.6, 86.6, 86.9, 87.2, 87.3, 87.7, 87.7, 87.7, 87.9, 88.5, 88.5, 88.6
University of Cincinnati College of Medicine		(1931)†	79.3, 79.4, 79.5, 80.5, 80.6, 81.1, 81.6, 81.6, 82, 82, 82.1, 82.1, 82.2, 82.3, 82.3, 82.4, 82.6, 82.8, 82.9, 83, 83, 83.1, 83.1, 83.1, 83.1, 83.3, 83.4, 83.6, 83.8, 83.8, 83.9, 83.9, 83.9, 84, 84.1, 84.1, 84.4, 84.4, 84.5, 84.6, 84.8, 84.9, 85.1, 85.3, 85.3, 85.4, 85.5, 85.5, 85.6, 85.8, 85.9, 85.9, 86.1, 86.3, 87, 87.5
Western Reserve University School of Medicine		(1931)	78.5, 78.5, 78.8, 80, 80, 80.4, 80.8, 80.8, 80.8, 80.9, 81.8, 82.4, 82.5, 82.5, 82.8, 83.1, 83.1, 83.2, 83.7, 83.7, 83.8, 83.8, 84, 84, 84, 84.2, 84.2, 84.3, 84.3, 84.4, 84.5, 84.5 84.9, 85, 85.1, 85.1, 85.2, 85.3, 85.3, 85.4, 85.4, 85.7, 85.8, 85.9, 85.9, 86, 86, 86.1, 86.6, 86.7, 86.7, 86.9, 87.3, 87.5, 88.4, 88.5
Jefferson Medical College of Philadelphia		(1930)	86.2
University of Pennsylvania School of Medicine		(1931)	76.7, 84, 85, 86.3
Meharry Medical College		(1930)	77.3
Vanderbilt University School of Medicine		(1930)	84.1
Medical College of Virginia		(1930)	83.3
Marquette University School of Medicine		(1931)	85.1
Dalhousie University Faculty of Medicine		(1925)	79.7
Queen's University Faculty of Medicine		(1928)	77.5
University of Toronto Faculty of Medicine		(1928)	85.2, (1930) 82.9, 83.6
University of Edinburgh Faculty of Medicine		(1925)	79.4

College	FAILED	Year Grad.	Per Cent
Laval University Faculty of Medicine		(1928)	74.3
University of Athens School of Medicine		(1917)	60.8
University of Budapest Faculty of Medicine		(1926)	58.4
University of Florence Faculty of Med. and Surg.		(1927)‡	72.1
University of Naples Faculty of Medicine		(1930)‡	56.8

Dr. Platter also reports 48 physicians licensed by reciprocity with other states and one physician licensed by endorsement, July 7, 1931. The following colleges were represented:

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1927)	Arkansas
University of Colorado School of Medicine		(1930)	Colorado
Howard University School of Medicine		(1930, 3)	Kansas
University of Georgia Medical Department		(1921), (1930)	Georgia
Rush Medical College		(1916), (1931)	Illinois
Indiana University School of Medicine		(1928), (1930)	Indiana
University of Indianapolis Medical Department		(1903)	Indiana
University of Kansas School of Medicine		(1930)	Kansas
University of Louisville Medical Department		(1920)	Kentucky
University of Louisville School of Medicine		(1930, 5)	Kentucky
Tulane University of Louisiana School of Medicine		(1924)	Arizona
Bowdoin Medical School, Maine		(1910)	Maine
Boston University School of Medicine		(1909)	Texas
Harvard University Medical School		(1927)	New York, N. Carolina
Detroit College of Medicine and Surgery		(1926), (1931, 2)	Michigan
University of Michigan Medical School		(1923), (1927, 2), (1929), (1930, 4)	Michigan
St. Louis University School of Medicine		(1930, 2)	Missouri
Creighton University School of Medicine		(1930)	Kansas
University and Bellevue Hospital Medical College		(1930)	W. Virginia
University of Oregon Medical School		(1928)	Oregon
Jefferson Medical College of Philadelphia		(1909)	Penna.
Meharry Medical College		(1922) Mississippi, (1927)	New York
University of Tennessee College of Medicine		(1930)	Tennessee
Vanderbilt University School of Medicine		(1929), (1930)	Tennessee
University of Virginia Department of Medicine		(1924)	Virginia
University of Toronto Faculty of Medicine		(1927)	Michigan

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1925)	N. B. M. Ex.

* No grade given. The M.D. degree and license of one of these applicants is being withheld pending completion of an internship.

† These applicants have received their M.B. degree and will receive their M.D. degree on completion of an internship.

‡ Verification of graduation in process.

Maine November Report

Dr. Adam P. Leighton, Jr., secretary, Maine Board of Registration of Medicine, reports the written examination held at Portland, Nov. 12-13, 1931. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Seven candidates were examined, all of whom passed. Two physicians were licensed by reciprocity with other states and two physicians were licensed by the endorsement of credentials. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
Johns Hopkins University School of Medicine		(1898)	82
Boston University School of Medicine		(1931)	84
Harvard University Medical School		(1929) 82, (1931)	85
Tufts College Medical School		(1931)	84, 88
Laval University Faculty of Medicine		(1931)	84

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Columbia University College of Phys. and Surg.		(1899)	Colorado
University of Vermont College of Medicine		(1919)	Vermont

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1930, 2)	N. B. M. Ex.

Pennsylvania Reciprocity Report

Mr. Charles D. Koch, secretary, Pennsylvania State Board of Medical Education and Licensure, Department of Public Instruction, reports 6 physicians licensed by reciprocity with other states and 5 physicians licensed by endorsement of credentials from Aug. 26 to Dec. 10, 1931. The following colleges were represented:

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Rush Medical College		(1919)	Illinois
University of Michigan Medical School		(1930)	Michigan
University of Minnesota Medical School		(1928)	Minnesota
Ohio State University College of Medicine		(1927)	Florida
Jefferson Medical College of Philadelphia		(1915)	N. Carolina, (1925) Minnesota

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Michigan Medical School		(1926)	N. B. M. Ex.
Jefferson Medical College of Philadelphia		(1930)	N. B. M. Ex.
University of Pennsylvania School of Med.		(1929), (1930)	N. B. M. Ex.
University of Pittsburgh School of Medicine		(1930)	N. B. M. Ex.

South Carolina November Report

Dr. A. Earle Boozer, secretary, South Carolina State Board of Medical Examiners, reports the oral examination held at Columbia, Nov. 10-12, 1931. The examination covered 17 subjects and included 100 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. One physician was licensed by reciprocity and one physician was licensed by endorsement of credentials. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
Howard University School of Medicine		(1931)	75
University of Tennessee College of Medicine		(1925)	79.4

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Georgia Medical Department		(1925)	Georgia

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Virginia Department of Medicine		(1926)	N. B. M. Ex.

Book Notices

Medicine in Virginia in the Eighteenth Century. By Wyndham B. Blanton, M.D. Cloth. Price, $7.50. Pp. 449, with illustrations. Richmond: Garrett & Massie, Inc., 1931.

The eighteenth century saw the rise of Russia and Prussia and the gathering of forces that led to the French Revolution. England experienced tremendous colonial expansion. There were wars in Europe, Asia, America and on the seas, corrupt morals, the South Sea bubble, the rise of Wesleyanism, and finally an aroused moral sense. To one group of historians, the spirit of the century was humanitarian idealism. They see interest in child welfare, the birth of pediatrics, and a great increase in the number of hospitals. Other historians see the rise of the arts and sciences; histology, pathology and physiology assumed the rôle of new sciences; disease entities were more clearly defined under keen clinical observation. Some historians are impressed only by the intellectual muddling of the eighteenth century's scientific men, and their great output of ridiculous theories. The surgical center of gravity shifted from France to England; Hunter, Pott and Guy came on the scene. The rise of histology under Bichat, of pathology under Morgagni, of physiology under Haller, and of vaccination under Jenner were reflected in America. There was here the same fondness for theories in medicine that Europe had. Then the most popular theories were those of Sydenham, who taught that morbific matter was fundamental in the cause of disease. Nature in an endeavor to expel the injurious substance from the body produced symptoms and signs. Sydenham believed that to cure disease this morbific matter must be discharged through the sweat, in the stools and in cutaneous eruptions. The theories of Boerhaave, which, Benjamin Rush said, governed the practice of every Philadelphia physician, accepted what was good in all other theories of the time. The cause of disease was sought for and found in the movements of the heavenly bodies. Fever was an effort of nature to put off death, inflammation was the mechanical obstruction of the capillaries, and the circulation and digestion could be explained on mechanical principles. Boerhaave recognized three diatheses: salt, putrid and oily temperaments. His therapy was the debilitating use of phlebotomy and purges. William Cullen, under whom many Virginians studied in Edinburgh, sponsored a theory known as solidism, which was predicated on a dynamic something called "nerve principle," which was supposed to produce spasm and atony. Cullen enjoined simplicity in therapeutics and opposed phlebotomy. The theory of John Brown of Edinburgh, who also influenced America, was based on the assumption that all living tissue is excitable. If this function of the tissue was increased, the result was sthenic diseases; if decreased, the result was asthenic diseases. His system of therapeutics was simply to depress or stimulate, as the case required. Alcohol and opium were the favorite therapeutic agents of this school. Thus we see the background for the education of physicians in America, many of whom at that time went abroad to study.

The Virginia doctor continued to sweat, blister, purge, vomit and bleed his patients. The mainstays of treatment were calomel, opium, ipecac and the famous rattlesnake root, each being given by the plantationers and doctor alike with confidence. The finest anatomist of the time was William Baynham, who, although practicing surgery in rural Virginia, had a national reputation. While studying at St. Thomas in London, he demonstrated, for the first time, "a fine vascular membrane immediately below the malpighian layer of the skin, separate and distinct from the cutis and capable of separation from it throughout its whole extent." Baynham mastered the fine technic of vascular injection as few others did. As a surgeon, he had the same standing as John Hunter, Pott and Abernethy. He was summoned far and wide in spite of eccentricities of temper and an exterior gloomy and austere. He was neither gracious nor talkative and none too distinct in the enunciation of his ideas.

Equally bold as a surgeon in Virginia was Jesse Bennett, who in 1794 performed a cesarean section on his wife and removed both ovaries. This, the first operation of its kind in America, was done thirty-three years previous to a similar operation by John Richmond, who, Garrison says, performed the first cesarean section in this country at Newtown, Ohio, in 1827. Bennett was not given the place of honor in history because he did not report his case in a medical journal. When asked why, he replied that "no doctor with any feelings of delicacy would report an operation he had done on his own wife, no strange doctors would believe that the operation could be done in the Virginia backwoods and the mother live, and he'd be damned if he would give them a chance to call him a liar." This historic operation by Bennett followed a difficult labor, due to a contracted pelvis in which forceps had been tried without success. The case was urgent, and Bennett decided that he himself would operate. The patient, stretched on a crude plank table over two barrels, was put under the influence of a large dose of opium. Bennett was assisted only by two Negro women. With one stroke of the knife he laid open the abdomen and uterus. He quickly delivered the child and placenta, and delayed long enough to remove both ovaries. He closed the wounds with stout linen thread, and Mrs. Bennett promptly recovered. The child, a daughter, lived to be 77 years of age. The oophorectomy performed by Bennett on his wife antedated McDowell's famous operation on Mrs. Crawford by more than fifteen years. Bennett thereafter enjoyed an extensive reputation as a surgeon and two years later moved to a 9,000 acre tract on the Ohio River, where he became the first justice of Mason County and represented the county in the Virginia assembly. He was a witness in the trial of Aaron Burr, who tried to persuade him to join his ill fated expedition. Bennett was a surgeon in the War of 1812, as well as in the Whisky Rebellion. He died, July 13, 1842, at Riverview, Mason County, Virginia. Another eminent surgeon of the time was Thomas Walker, who is said to have been the first in this country to trephine bone for suppurative osteomyelitis.

The eighteenth century was notable in obstetrics for the popularizing of the forceps and the return of the male midwife. It was not until the latter part of the century that men seriously disputed the position of midwives in their field in America. In Virginia, a new influence was felt when the young men trained in Europe, where obstetrics for the first time was receiving serious attention, returned to practice. Andrew Anderson advertised himself in Williamsburg as "surgeon and man-midwife." In spite of the physician's entrance into the practice of obstetrics, child bearing in Virginia in the eighteenth century was fraught with danger, and the ordeal of birth, although almost a yearly event in many families, was anticipated with misgiving. Dr. George French of Fredericksburg, however, had a patient who in 1799, at the age of 40, was the mother of twenty-one children and after that date gave birth to three more. According to Dr. French, she belonged to "one of the first families in the country."

In discussing medical fees in Virginia, the authors illustrate the cost of living by citing some prices. A horse cost from £2 to £3, a feather-bed, from £1 to £3, and a coat and waistcoat, £2. Dr. John Bowman rendered a bill for 120 pounds of tobacco to one estate; Dr. Joshue Irby asked 10 shillings for a single visit and once (for salivating a Negro) he received 2,000 pounds of tobacco. Dr. William Cabell charged from £1 to £5 a visit, according to the distance, and for amputating an arm or leg, £7 10s. One who traveled in Virginia in the eighteenth century said: "I have heard physicians declare that they do not annually receive one third of what is due to them for their attendance; that they have some of these debts of five and twenty years' standing; that their claims are frequently denied, and that in order to recover payment they are obliged to send, write, carry on lawsuits, etc." This writer added that lawyers were well paid.

The drug business in Virginia during the eighteenth century was largely in the hands of physicians, some of whom set up apothecary shops of their own, a practice that in some places still exists. The first physician to make a practice of writing prescriptions in America was Abraham Chauvet, who came to Philadelphia in 1770 and boldly gave up peddling his own medicine. Newspaper advertising was extensively used by the drug houses conducted by physicians; competition was keen. Rival concerns were accused of spreading scandalous and groundless reports about each others' wares. Dr. George Pitt of Williamsburg conducted an apothecary shop called "The Sign

of the Rhinoceros"; his small brick building, which still stands, is thought to be the oldest apothecary shop in the country. Dr. James Carter of Williamsburg conducted an apothecary shop which he called "The Unicorn's Horn." He retired from the apothecary business in 1779 but continued to practice medicine in Williamsburg until his death.

In the eighteenth century, an apothecary shop was an interesting place. Over the door hung a conventional sign—A golden ball, a mortar and pestle, a dragon or deer, or a dove. In the window were the colored carboys. The atmosphere was pungent with odors of spices, fumes of volatile drugs, or the by-products of the distillation that was always going on. Around the walls were rows of jars and demijohns; there was a massive prescription counter with large brass scales, the clumsy strainer, the great stone mortar, the press and the shiny pill tile. "Patent medicines" were prominently displayed. The apothecary shop was a gathering place of the local notables, as well as a museum of ancient practices of pharmacy.

New York, Philadelphia, Charleston, Baltimore and other seaports had epidemics of yellow fever. The earliest epidemics in Virginia, in 1737, were described by Dr. John Mitchell, who attended about thirty cases along the lower Rappahannock River. When the great epidemic was raging in Philadelphia in 1793, Virginia resorted to strict quarantine laws as a safeguard against yellow fever. The governor issued a proclamation which required all ships from Philadelphia to anchor at a certain place and passengers were forbidden to land for twenty days. In 1795, an epidemic of yellow fever occurred in Norfolk causing 220 deaths in six weeks.

Smallpox periodically assumed epidemic proportions. In Virginia as well as in Europe and other places there was at first great opposition to inoculation and vaccination against smallpox. An epidemic in Williamsburg in 1768 was attributed to inoculation. An act was passed in 1770 to penalize any one wilfully importing variolous matter with the intention of inoculating. Seven years later this act was amended to permit inoculation if the consent of the housekeepers within the radius of two miles was first obtained. Virginia's attitude toward vaccination was more creditable, thanks chiefly to Thomas Jefferson, whose part in popularizing the procedure by experimenting on his slaves at Monticello and by giving the virus to physicians in different parts of the country has never been fully appreciated. During the revolutionary period, Washington ordered his troops inoculated and set apart houses to be used for inoculation hospitals. The devastation of smallpox among the uninoculated troops was frightful, but Virginia troops were relatively free of smallpox until the Yorktown campaign.

We are told that the majority of American physicians relied for their medical education on the system of apprenticeships. No doubt many excellent doctors came out of these schools of experience, but the opportunity for fraud was great. Ignorant men were to be found who claimed to have studied under eminent masters. Doctors with degrees heaped on the general run of apprentice-trained physicians the indictment of quackery. A medical department was organized at the College of William and Mary, but it functioned only three years.

Despite the difficulty of obtaining books, there were some private medical libraries; one of the largest, that of Col. William Fleming, who practiced in Botetourt County, included forty-three works on medicine. The titles of these books are listed in this volume. Dr. John Sutherland of Spotsylvania County left in his will, filed in 1763, 163 books, of which 67 were devoted to medicine.

The general public in the eighteenth century had a keen interest in medical science. Medicine in Virginia owed a debt to men outside the profession, notably to William Byrd II and Thomas Jefferson. Byrd, a man of wealth, typified the non-professional interest in medicine. Jefferson enjoyed a position of even greater power and influence. Jefferson made a lasting contribution in establishing at the University of Virginia a chair of medicine. In his library were many medical books. He undoubtedly practiced on himself and his family of Negroes.

The Revolutionary War brought some benefits to the medical profession in America. Well trained European surgeons remained in America after the war. American surgeons by watching the French, German and English surgeons learned valuable lessons. Dr. James Madison, writing to his father from Williamsburg, said: "We had the other day the satisfaction of seeing the greatest respect paid to our university. Dr. Coste, the first physician to the French army, delivered a Latin oration on medicine in general, with application to this country, and you will probably soon see it in print in Philadelphia." The Revolution enabled American physicians to broaden their knowledge by travel and association and to set up better standards of practice. No Virginian rose to the supreme command of the medical forces of the Revolution; many, however, attained high positions and some were generals in the line. Dr. Adams Stephen became one of Virginia's three major generals and Hugh Mercer became a brigadier general; Dr. Theodorick Bland was a colonel of cavalry and Dr. William Lewis a colonel of infantry. It is interesting to recall the diseases which gave the Revolutionary Army trouble. Congress, in 1778, in an effort to diminish venereal disease issued an order to the effect that $10 should be paid by every officer and $4 by every soldier who was sent to any hospital to be cured of venereal disease, and those sums were to be deducted from their pay. Benjamin Rush declared that "the principal diseases in the hospitals were the typhus gravior and mitior of Dr. Cullen. Men who came into the hospitals with pleurisies or rheumatisms soon lost the types of their original diseases and suffered, or died, by the above mentioned states of fever. The contagion of this fever was frequently conveyed from the hospital to the camp by means of blankets and clothes." This disease was then called jail fever, also putrid fever. It probably was typhus, but since no distinction was made between typhoid and typhus, it is difficult to say which was actually responsible for the epidemics.

Washington directed Dr. James Craik, the physician general, to provide a separate hospital for smallpox at Williamsburg. That smallpox was not more serious during the Revolutionary War was due to unusual precautions to prevent it by inoculation, for which no one was more responsible than George Washington. Malaria was particularly troublesome in the South. Congress in 1776 ordered that 300 pounds of Peruvian bark be sent to the southern department for the use of the troops.

The first marine hospital established under an act of Congress was purchased from Virginia by the government in 1800. This hospital was operated by the government until the Civil War, when the Confederates used it for barracks. It later fell into federal hands and was converted by them into an army hospital. It was finally sold in 1875 under an act of Congress, which provided for the sale of all marine hospitals whose admission rate fell below a certain point. The building is still standing at Ferry Point in Norfolk County, although alterations have greatly changed its appearance. This marked the beginning by the U. S. government of a service toward men of the sea that has expanded until today there are twenty-six first class marine hospitals in the United States, attending annually nearly 400,000 patients. This service grew out of a condition among sailors that was pitiable. In 1801 there were not less than 3,000 American sailors entering the port of New Orleans alone, without money or friends, careless, reckless, exposed to hardships. They often were exposed to epidemic or deficiency diseases. The plight of sailors finally aroused the nation to action in 1798, when Congress decided to provide for a marine hospital service.

Some of George Washington's greatest friends were physicians. Dr. David Stuart married the widow of John Custis, Mrs. Washington's son. Washington appointed Dr. Stuart one of the first commissioners of the District of Columbia and in 1791 he and Daniel Carroll of Maryland established the boundary line of the district. Dr. James Craik was Washington's intimate friend. Dr. Craik was the kind of man Washington liked, modest, efficient and fond of the outdoors. A physician who served under Craik at Yorktown declared that his professional merits were of the highest order and "that his memory is precious to all who had the happiness and the honor of acquaintance." Craik came to this country from Scotland at the age of 20. He is said to have been an illegitimate son but was acknowledged and protected by his father, Robert Craik, a member of parliament. His father had a gardener by the name of John Paul, whose son migrated to Virginia, took the name of John Paul Jones and became "the founder of the American Navy." Dr. Craik became the physician-general of the Revolutionary forces. After the war he took up his resi-

dence, at Washington's suggestion, at Alexandria, Va., a short distance from Mount Vernon, where he was a constant visitor. Craik was the first physician to come to Washington's death bed. The chapter on Washington's last illness has been told before. It may not be generally known that Washington was not as robust as the public believed him to be. He was large and sinewy but had a bad inheritance. His paternal forefathers were short lived and among the ancestors was a marked tendency to pulmonary disease. Washington is said to have been afflicted with "a malignant tumor of the thigh, called anthrax at the time, but really a carbuncle," which threatened his life scarcely six weeks after he became president. He was subject to colds and several times had dysentery. He was constantly attended by dentists, and having lost one tooth after another, untimately had to wear complete sets of false teeth. At 46, Washington began to use eyeglasses. Toward the end of his life he also became quite deaf. After 1793, those near him believed that he heard but little of the conversation around him. Washington's death was unexpected; it was attended by unusual circumstances and was followed by a wave of calumny that spent its fury chiefly on the medical profession. Some said he died of diphtheria, some of quinsy. His attending physician called the disease cynanche trachealis.

The remainder of this charming history comprises a brief biography of many physicians in Virginia towns. These are taken up under such subjects as the three capitals, Jamestown, Williamsburg and Richmond; country doctors, tidewater physicians, middle Virginia physicians, Piedmont physicians, transalleghany physicians, and finally a chapter on medical legislation. The wave of interest which within a few years has brought forth several volumes of medical histories of the states has produced none more interesting or more attractive than "Medicine in Virginia in the Eighteenth Century," by Wyndham B. Blanton, Beverley R. Tucker and Frederick C. Rinker, who comprise the historical committee of the Medical Society of Virginia.

Diseases of the Stomach. By Hugh Morton, M.D. Cloth. Price, $4. Pp. 184, with illustrations. New York: Longmans, Green & Company; London: Edward Arnold & Company, 1931.

The author has written a short book in which the more important points relevant to the etiology, morbid anatomy, symptomatology, physical examination, laboratory observations, roentgen manifestations and prognosis of the various diseases of the stomach are discussed. The sections on treatment are particularly good; they contain useful prescriptions and from time to time the author's individual methods of procedure. Illustrative cases encountered by the author are effectively interspersed. In the treatment of cardiospasm, no mention is made of the use of esophageal bougies. The last chapter is devoted to the chemical methods of value in the diagnosis of gastric disease; the Wohlgemuth test for pancreatic function and the van den Bergh test are included. Unfortunately, the histamine test, so useful in the differentiation of spurious or functional achlorhydria from true achlorhydria, is omitted. While on the whole the book is written in a clear, direct style, the author at times grows careless in his diction and grammatical structure. There appears to be an inordinate number of typographic errors. In the dosage of hydrochloric acid, nux vomica and cerium oxalate, page 24, there is a typographic error, 2 ounces appearing instead of 2 drachms. In general, however, the book should prove a useful guide to the busy practitioner.

Illustrated Primer on Fractures. Prepared by the Cooperative Committee on Fractures under Auspices of Section on Surgery, General and Abdominal, and Section on Orthopedic Surgery in Cooperation with Department of Scientific Exhibit of the American Medical Association. Second edition, revised and reedited. Cloth. Price, $1. Pp. 63, with illustrations. Chicago: American Medical Association, 1931.

In the second edition, this valuable primer has been entirely revised and reedited. It is emphasized that the purpose of the primer is not to standardize the treatment of fractures but to suggest what, in the opinion of the cooperative committee on fractures, constitute acceptable methods of treatment. Blank pages are interspersed so that the student may make notes to amplify the material presented by the instructor. Four new topics are included in this edition: compression fracture of the spine, fracture of the skull, active movements in the treatment of fractures, and massage during the treatment of fractures. The book begins with how to make plaster-of-paris bandages and ends with splints and accessories for the doctor's automobile and office. The illustrations are effective. Many of the statements, epigrams and admonitions printed in large type are excellent. The primer was not intended to be an encyclopedia of the treatment of fractures. It does not discuss the unusual cases, but it is an excellent guide in the treatment of the common fractures. It is good value for the money it costs and can be recommended without reserve to every medical student, intern and general practitioner.

Précis de bactériologie médicale. Par André Philibert, professeur agrégé de bactériologie à la Faculté de médecine de Paris. Second edition. Cloth. Price, 65 francs. Pp. 551, with 21 illustrations. Paris: Masson & Cie, 1931.

This book is designed to cover methods for bacteriologic examination of body secretions and excretions as well as to present descriptions of pathogenic micro-organisms, together with characteristics useful for identification. Many of the methods are indicated rather than described in minute detail, so that the material will be useful for trained laboratory workers rather than for beginners. The illustrations are in color and, in general, are excellent.

Pettibone's Textbook of Physiological Chemistry with Experiments. Revised and rewritten by J. F. McClendon, Ph.D., Professor of Physiological Chemistry, Medical School, University of Minnesota, Minneapolis. Fifth edition. Cloth. Price, $3.75. Pp. 370, with 18 illustrations. St. Louis: C. V. Mosby Company, 1931.

This book was prepared as an intermediate work to cover the general field of physiologic chemistry, and it developed out of courses given in the subject by a number of men. It has therefore withstood the test of experience. Its size commends it to the student and to teachers, who should know the volume of information to expect from a student. It is divided into two parts, one devoted to the discussion of the subject (222 pages) and the other to laboratory experiments. The introduction is brief and pointed. The principles of physical chemistry are given thirty-eight well written pages. Salts and water, fats and allied substances, carbohydrates, proteins, vitamins, some important foodstuffs and diet, absorption and digestion, the urine, and metabolism are discussed. Necessarily, the discussion and chemical formulation are brief. Few books could compete with this one in the presentation of the subject with so small a number of chemical formulas. The laboratory work occupies 110 pages, is well selected, and quite comprehensive. A list of references to books and important contributions is appended. In these times, when the medical curriculum is overloaded, this book is a courageous attempt to lessen the load and to present the essentials of physiologic chemistry in a brief but adequate manner.

Die Behandlung der Kinderkrankheiten mit Ultraviolett- und Röntgenstrahlen. Von Prof. Dr. W. Birk, Vorstand der Universitäts-Kinderklinik in Tübingen, und Dr. L. Schall, Chefarzt der Kinderabteilung am Landeskrankenhaus Homburg-Saar. Band XVII. Sonderbände zur Strahlentherapie. Herausgegeben von Professor Dr. Hans Meyer. Second edition of "Strahlenbehandlung bei Kinderkrankheiten" published in 1924. Paper. Price, 12 marks. Pp. 256, with 45 illustrations. Berlin: Urban & Schwarzenberg, 1932.

The increasing recognition of the importance of ray therapy in treating children's diseases induced the authors to rewrite their textbook in order to adjust it to the latest accomplishments in this line of work. In an introductory chapter the physical fundamentals of ultraviolet rays are discussed. This is followed by a discussion of the various appliances to be used in the production of these rays, the dosages and the possible injurious influences, and their prevention. A welcome addition is the discussion of the relation of ultraviolet rays, cod liver oil and vitamin D. The indications for this therapy in the various diseases of infants and the possible results are thoroughly explained. A special chapter is devoted to the application of this modality to the various manifestations of tuberculosis in infants. The second part of this book is devoted to the discussion of roentgen therapy. Again at first the technic is discussed, followed by a thorough presentation of the clinical possibilities of the method, covering all the instances in which it may be employed successfully. This publication is a thoroughly reliable guide for any one who takes an interest in this branch of pediatrics.

Living the Liver Diet. By Elmer A. Miner, M.D. With introduction by William P. Murphy, M.D., Instructor in Medicine at the Harvard Medical School, Boston. Cloth. Price, $1.50. Pp. 106. St. Louis: C. V. Mosby Company, 1931.

This volume, written by a physician who has pernicious anemia, is "for the pernicious anemia patient, for the busy physician to use as a handbook on the liver diet, for any one desiring a reducing diet, and for any one desiring good health." The author properly states that successful results are obtained in the treatment of pernicious anemia only when the physician obtains the intelligent cooperation of the patient. Too much emphasis, however, is placed on the original liver diet introduced in 1926, which contained directions concerning the use of liver, fruits, red muscle meat, vegetables, and a reduction in the amount of fats. While whole liver will always have a place in the treatment of pernicious anemia, a large amount of careful scientific work has demonstrated that the use of a potent liver extract or desiccated hog's stomach, combined with an average diet which the patient may select without direction, produces highly satisfactory results. The latter plan, moreover, has the great advantage of simplicity. The book contains chapters on liver, fruits, meat, vegetables, fats, sweets, starches, seasoning, drinks and the diet maintained. There are several standard tables showing the vitamin and caloric content of foods and a number of recipes for the preparation of liver.

English-Speaking Students of Medicine at the University of Leyden. By R. W. Innes Smith, M.D. With foreword by John D. Comrie, M.D., F.R.C.P., Lecturer on the History of Medicine at the University of Edinburgh. Cloth. Price, 16/–. Pp. 258. Edinburgh: Oliver & Boyd, 1932.

In the foreword, Comrie describes the work thus: "Dr. Innes Smith has taken the Album of Students at Leyden University from 1575 to 1875 as the basis of his investigations. After selecting those students who were engaged in medical study, he has traced them through the other universities scattered over Holland, France, Italy, and the home countries at which they graduated, and he has followed them into later life and discovered many important and interesting facts in regard to them which have not already been matters of general knowledge." The ten pages of introduction by the author give an interesting account of the universities of the low countries. The remainder of the book contains an alphabetical list of the students in question presented in this style:

Monro (Mouro) Alexander.—Scoto-Brittaunus, Nov. 16, 1780, Aet. 20, Med.—M.D., Edin., 1756. F.R.S., 1723. F.C.C.P., Edin., 1756. Professor of Anatomy at Edin. Univ. Well known as "Monro Primus." Born 1697. S. of John (vide). Died 1767. Vide *D.N.B.*

There are 258 pages of such names, with a biographic account in keeping with the importance of the person. In view of the immense amount of labor necessary to issue this volume, it is hoped that the book will be found useful to students of medical history.

Recent Advances in the Study of Rheumatism. By Frederic John Poynton, M.D., F.R.C.P., Physician, University College Hospital, and Bernard Schlesinger, M.A., M.D., M.R.C.P., Physician to the Children's Department, Royal Northern Hospital. Cloth. Price, $3.50. Pp. 313, with 25 illustrations. Philadelphia: P. Blakiston's Son & Company, Inc., 1931.

The names of the authors are familiar to all students of the literature on rheumatism. They are accurate observers and good clinicians. They have written much that has stood the test of time. One of the authors was a pioneer in the recognition of the importance of focal infection in relation to systemic disease. The book is small. The material is well chosen and in good sequence and it is easily read. Unfortunately, it does not tell how to treat cases of rheumatism. The author gives in detail his experience with nirvanol, which he regards as a valuable agent. The book contains a good bibliography. It should be valuable to the internist and specialist.

La estenosis dextroventricular (sindrome de Bernheim). Por los Doctores Tullo Martini, jefe de sala del Hospital Rawson, y Miguel Joselevich, jefe de clínica de la facultad y del servicio. Paper. Pp. 129, with 34 illustrations. Buenos Aires: E. Spinelli, 1931.

This syndrome was first described by Bernheim in 1906, and this book is written in order to acquaint the medical profession with this rare condition. It refers to a stenosis of the right ventricle accompanied by a dilatation and hypertrophy of the left ventricle and right auricle. In extreme instances, the stenosis is so great that the right ventricle appears as an appendage of the heart. Mitral and aortic insufficiencies and chronic myocarditis predispose; clinically there are signs of cardiac embarrassment, and in the electrocardiograph a left ventricular predominance is noted. The lesion can be best demonstrated at necropsy by making four transverse cuts: one through the auricles and three through the ventricles of the heart.

Medicolegal

When Does Treatment Cease?

(Schmitt v. Esser (Minn.), 236 N. W. 622)

The physician-defendant was employed by the plaintiff, March 5, 1926, to treat her broken and dislocated ankle. On April 5 he cut open the cast, examined the injured joint, and gave instructions as to its care, advising his patient to remain in bed for three weeks and then to get up and walk. At the end of that period she was unable to walk without the aid of crutches. On July 3 she summoned the physician-defendant, who came and watched her walk. In August she visited him at his office, where he examined her foot. She visited his office several times after that, but no further examination of the foot was made. The plaintiff contended that the physician-defendant told her that the fracture required two years in which to heal and that she did not discover the falsity of that statement until June 1, 1928. She then sued, summons being served, June 5, 1928. The physician-defendant demurred, claiming that the action was barred by the statute of limitations. From an order of the district court, Otter Tail County, overruling the demurrer, he carried the case to the Supreme Court of Minnesota, on questions certified as important and doubtful.[1]

In malpractice cases, said the Supreme Court, there is difficulty in determining the precise moment when the act or omission which caused the damage took place. It may have occurred at some particular moment or it may have persisted and characterized the whole course of treatment. It would seem advisable, therefore, not to apply the bar of the statute of limitations on demurrer, unless it clearly appears from the complaint that the unskilful or negligent act that caused the injury took place more than two years before the action was brought. The physician-defendant contended, however, that where the malpractice charged is failure to set a fracture, and when the complaint shows that after the fracture was set and before the service of the summons the statute of limitations has run, a demurrer based on the statute is properly sustained. The Supreme Court, however, adopted the view of the Supreme Court of Ohio in *Bowers* v. *Santee*, 124 N. E. 238, holding that the statute of limitations in an action in contract by a patient against his physician, based on alleged malpractice, does not begin to run until the relation of physician and patient terminates. We think, said the Supreme Court of Minnesota at that time, the treatment and employment should be considered as a whole, and if malpractice occurs the statute of limitations begins to run "when the treatment ceases." The order of the trial court overruling the demurrer of the physician-defendant was therefore affirmed and the case was tried on its merits in the district court. A verdict was rendered for the plaintiff. The physician-defendant then filed a motion for a judgment in his favor or a new trial, and from an order denying his motion he appealed again to the Supreme Court of Minnesota. On this appeal, said the Supreme Court, the question is whether under the evidence introduced the action was barred.

Where a physician is employed generally to treat and heal an injury, said the Supreme Court, he owes the duty of giving continued care and treatment. If the jury found that the physician-defendant was negligent in failing to apply proper treatment in July and August, 1926, this action, which was commenced on June 5, 1928, would not be barred. When the case was before the court on the former appeal the court concluded that when malpractice occurs the statute of limitations begins to run "when the treatment ceases." But negligent failure to treat, when the need of treatment is known to the

1. Schmitt v. Esser (Minn.), 226 N. W. 196, J. A. M. A. **94**: 568 (Feb. 22) 1930.

attending physician and there is opportunity to apply proper treatment, is the same as negligent treatment. The question is, When does treatment cease? It cannot be said that treatment has ceased as long as the relation of physician and patient continues as to the particular injury or malady which the physician is employed to cure, the physician continues to attend and examine the patient in relation thereto, and there is something more to be done by the physician to effect a cure. There need be no formal discharge of the physician nor any formal termination of his employment; if there is nothing more for the physician to do as to the particular injury or malady which he was employed to treat or if he ceases to attend the patient for it, the treatment ordinarily ceases without any formality.

When this case was before the Supreme Court on a previous occasion, *Schmitt* v. *Esser*, 226 N. W. 196, the court held that the statute of limitations begins to run "when the *treatment* ceases." In the trial of the case, however, the trial court charged the jury that if it found that *the relation of physician and patient between the parties* terminated on or prior to June 3, 1926, it should find a verdict for the physician-defendant, and otherwise for the plaintiff. The court gave the jury no information as to what would constitute a termination of the relation of physician and patient. Termination of treatment does not necessarily depend on the termination of the relation between physician and patient; treatment of a particular ailment or injury might terminate and the relation of physician and patient nevertheless continue. The test applied in the trial court was not the test prescribed by the Supreme Court in its previous decision. The jury might conclude, under the instructions given, that the relation of physician and patient continued until and unless there was a discharge of the physician or some word or act on his part clearly showing a termination, notwithstanding the fact that treatment of the injury might have terminated long before. The charge of the trial judge constituted, therefore, in the judgment of the Supreme Court, prejudicial error.

A physician testifying on behalf of the plaintiff was permitted to state the stand or action that certain medical associations had taken with reference to the right of a physician to testify in a negligence or a malpractice case. At least as coming from the plaintiff's own witness, said the Supreme Court, it was error to go into that question. Another witness was permitted, over objection, to give testimony on the same subject. This also was error.

The order of the trial court was reversed and a new trial granted.

Accident and Health Insurance: Hernia an Accidental Injury or Sickness.—The defendant insurance company insured the deceased against loss of life resulting solely through accidental means and provided for the payment of certain weekly indemnities for disability caused by sickness. The insurance policy provided that "disability resulting wholly or partly from . . . hernia . . . shall be considered as sickness and indemnified under the sickness provision of the policy whatever the original cause." The insured suffered a traumatic hernia as the result of a fall. An operation was performed, acute dilatation of the stomach set in, and he died. The beneficiary under the policy waived all claims for sickness indemnity and sought to recover the amount payable for death caused by accidental means. The trial court directed a verdict in favor of the insurance company, holding that recovery could be had only for sickness indemnity, since the deceased had suffered a disability resulting wholly or partly from hernia. The beneficiary thereupon appealed to the Supreme Court of Vermont. The beneficiary's evidence, said the Supreme Court of Vermont, tended to show that the hernia was caused by a fall; that is, by accidental means. Under such circumstances, death was attributable to the accident, and not to the hernia. The hernia was not a new and independent cause of death, but only a link in the chain of causation between the accident and the death. The jury, therefore, would have been justified in finding that death resulted from an accidental bodily injury, within the meaning of the policy. The operation, which the evidence tended to show was a proper step in the treatment, was not an intervening cause of death. Disability resulting from hernia, however it may have been caused, was classed by the policy as sickness, and the indemnities payable for sickness, not those payable for accident, were applicable. That, however, in no way affected the liability for the principal sum, for death caused solely by accidental means.—*Corsones v. Monarch Acc. Ins. Co. (Vt.), 154 Atl. 693.*

Society Proceedings

COMING MEETINGS

American Medical Association, New Orleans, May 9-13. Dr. Olin West, 535 North Dearborn Street, Chicago, Secretary.

Alabama, Medical Association of the State of, Mobile, April 19-22. Dr. D. L. Cannon, 519 Dexter Avenue, Montgomery, Secretary.

American Association for Thoracic Surgery, Ann Arbor, Mich., April 18-20. Dr. Duff S. Allen, 3720 Washington Blvd., St. Louis, Sec'y.

American Association of Pathologists and Bacteriologists, Philadelphia, April 28-29. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Bronchoscopic Society, Atlantic City, May 21. Dr. Richmond McKinney, 899 Madison Avenue, Memphis, Tennessee, Secretary.

American Climatological and Clinical Association, Atlantic City, May 5-7. Dr. Arthur K. Stone, Auburn Street, Framingham Center, Mass., Secretary.

American College of Physicians, San Francisco, April 4-8. Mr. E. R. Loveland, 133 South 36th Street, Philadelphia, Executive Secretary.

American Dermatological Association, Havana, Cuba, May 3-5. Dr. William H. Guy, 500 Penn Avenue, Pittsburgh, Secretary.

American Gastro-Enterological Association, Atlantic City, May 2-3. Dr. Charles G. Lucas, 307 West Broadway, Louisville, Secretary.

American Heart Association, New Orleans, May 10. Dr. Irl C. Riggin, 450 Seventh Avenue, New York, Executive Secretary.

American Laryngological Association, Atlantic City, May 19-21. Dr. George M. Coates, 1721 Pine Street, Philadelphia, Secretary.

American Otological Society, Atlantic City, May 17-19. Dr. Thomas J. Harris, 104 East 40th Street, New York, Secretary.

American Physiological Society, Philadelphia, April 28-30. Dr. Arno B. Luckhardt, 5216 Greenwood Avenue, Chicago, Secretary.

American Proctologic Society, Memphis, May 6-7. Dr. Curtice Rosser, 710 Medical Arts Building, Dallas, Texas, Secretary.

American Society for Clinical Investigation, Atlantic City, May 2. Dr. Cyrus C. Sturgis, Simpson Memorial Institute, Ann Arbor, Mich., Secretary.

American Society for Experimental Pathology, Philadelphia, April 28-30. Dr. C. Phillip Miller, Jr., University of Chicago, Chicago, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Philadelphia, April 27-30. Dr. V. E. Henderson, University of Toronto, Toronto, Secretary.

American Society of Biological Chemistry, Philadelphia, April 28-30. Dr. H. B. Lewis, University of Michigan Medical School, Ann Arbor, Secretary.

American Society of Clinical Pathologists, New Orleans, May 6-9. Dr. A. S. Giordano, 531 North Main Street, South Bend, Ind., Secretary.

American Surgical Association, New Haven, Conn., May 16-18. Dr. Vernon C. David, 59 East Madison Street, Chicago, Secretary.

American Therapeutic Society, Baltimore, May 16-17. Dr. Grafton Tyler Brown, 1801 I Street N.W., Washington, D. C., Secretary.

Arizona State Medical Association, Globe, April 21-23. Dr. D. F. Harbridge, 822 Professional Building, Phoenix, Secretary.

Arkansas Medical Society, Little Rock, April 5-7. Dr. William R. Bathurst, 814 Boyle Building, Little Rock, Secretary.

Association for the Study of Internal Secretions, New Orleans, May 9-10. Dr. F. M. Pottenger, 1930 Wilshire Boulevard, Los Angeles, Secretary.

Association of American Physicians, Atlantic City, May 3-4. Dr. James H. Means, Massachusetts General Hospital, Boston, Secretary.

California Medical Association, Pasadena, May 2-5. Dr. Emma W. Pope, 450 Sutter Street, San Francisco, Secretary.

District of Columbia, Medical Society of the, Washington, D. C., May 4-5. Dr. C. B. Conklin, 1718 M Street, N. W., Washington, D. C., Secretary.

Florida Medical Association, Sarasota, May 3-4. Dr. Shaler Richardson, 111 West Adams Street, Jacksonville, Secretary.

Georgia, Medical Association of, Savannah, May 17-20. Dr. Allen H. Bunce, 139 Forrest Avenue N.E., Atlanta, Secretary.

Illinois State Medical Society, Springfield, May 17-19. Dr. Harold M. Camp, 203 Lahl Building, Monmouth, Secretary.

Iowa State Medical Society, Sioux City, May 4-6. Dr. Robert L. Parker, 3510 Sixth Avenue, Des Moines, Secretary.

Kansas Medical Society, Kansas City, May 3-5. Dr. J. F. Hassig, 804 Huron Building, Kansas City, Secretary.

Louisiana State Medical Society, New Orleans, May 9-10. Dr. P. T. Talbot, 1430 Tulane Avenue, New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, April 26-27. Dr. Walter Dent Wise, 1211 Cathedral Street, Baltimore, Secretary.

Medical Society of the Missouri Valley, Omaha, Neb., March 29-31. Dr. Joseph D. McCarthy, 107 South 17th Street, Omaha, Secretary.

Medical Women's National Association, New Orleans, May 8-9. Dr. Sylvia Allan, Winthrop College, Rock Hill, S. C., Secretary.

Mississippi State Medical Association, Jackson, April 12-14. Dr. T. M. Dye, Clarksdale, Secretary.

New Hampshire Medical Society, Manchester, May 17-18. Dr. D. E. Sullivan, 7 North State Street, Concord, Secretary.

North Carolina, Medical Society of the State of, Winston-Salem, April 18-20. Dr. L. B. McBrayer, Southern Pines, Secretary.

Ohio State Medical Association, Dayton, May 3-4. Mr. Don K. Martin, 131 East State Street, Columbus, Executive Secretary.

South Carolina Medical Association, Columbia, April 19-21. Dr. E. A. Hines, Seneca, Secretary.

Tennessee State Medical Association, Memphis, April 12-14. Dr. H. H. Shoulders, 706 Church Street, Nashville, Secretary.

Texas, State Medical Association of, Waco, May 5-7. Dr. Holman Taylor, Medical Arts Building, Fort Worth, Secretary.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American J. Obstetrics and Gynecology, St. Louis

23: 1-154 (Jan.) 1932

Therapeutic Abortion in Pulmonary Tuberculosis. C. B. Ingraham, Denver.—p. 1.
*Therapeutic and Diagnostic Value of Curettage in So-Called Functional Uterine Bleeding. S. H. Geist and O. Glassman, New York.—p. 14.
Modern Conception and Treatment of Uterine Bleeding. E. J. Miller, New Orleans.—p. 24.
Prevalent Hour of Stillbirth. J. V. de Porte, Albany, N. Y.—p. 31.
Prevention of Obstetric Complications by Diet and Exercise. A. W. Bingham, East Orange, N. J.—p. 38.
Anterior Pituitary Hormone in Cerebrospinal Fluid During Pregnancy. S. D. Soule and T. K. Brown, St. Louis.—p. 44.
Some Notes on Sterility Due to Obstruction in Uterine Tubes. H. Schmitz, Chicago.—p. 47.
*Origin of Ovarian Epithelium. W. S. Gardner, Baltimore.—p. 54.
Breech Presentations: Report of One Hundred and Seventy Cases. R. W. Mohler, Philadelphia.—p. 61.
Hysterotomy and Sterilization. A. M. Mendenhall, Indianapolis.—p. 67.
Postpartum Partial Anuria with Uremia and Fatal Upper Abdominal Hemorrhage: Report of Case with Necropsy Observations. E. C. Hamblen and D. O. Hamblin, University, Va.—p. 73.
Cystic Fibroid with Twisted Pedicle, Simulating an Ovarian Cyst. Mary Spivack and I. Pilot, Chicago.—p. 77.
*Comparative Study of Aschheim-Zondek and Mazer-Hoffman Tests for Early Pregnancy. P. B. Bland, A. First and P. Roeder, Philadelphia.—p. 83.
Obstetric Anesthesia and Analgesia with Sodium Isoamylethylbarbiturate and Nitrous Oxide-Oxygen. H. S. Ruth and N. F. Paxson, Philadelphia.—p. 90.
Uterine Abscess, Hysterectomy, Recovery. R. A. Lifvendahl, Chicago.—p. 97.
Fractured Pelvis in Obstetrics: With Report of Cases. W. Schumann, Baltimore.—p. 103.
Carcinoma Developing in Myomatous Uterus After Roentgen-Ray Menopause. Catharine MacFarlane, Philadelphia.—p. 108.
Syphilis of Fetus and New-Born Infant. F. L. Adair, Chicago.—p. 111.
Samuel Bard, the Author of First Textbook on Obstetrics Published in America. H. Thoms, New Haven, Conn.—p. 115.

Value of Curettage in Uterine Bleeding.—Geist and Glassman believe that neither from the type of bleeding, the duration of the symptoms nor the microscopic data can a definite prognosis be made as to the possibility of cure. It would seem, however, that in cases presenting a marked increase in gland content of cystic type with irregular distribution the possibility of cure by means of curettage is unlikely. Curettage may be of curative value in inflammatory cases, those with polypi or polypoid endometrium with scanty or normal gland content, or cases in which a subinvolution subsequent to a previously overlooked gravidity presents the clinical picture of a functional metrorrhagia. All patients (except the puberty cases) should be curetted and observed, as a first procedure, and if necessary, with a recurrence of symptoms, recuretted before more drastic steps are taken.

Origin of Ovarian Epithelium.—According to Gardner, the cells surrounding the ovum in the graafian follicles are undifferentiated cells that are capable of developing in more than one way. Under what may be called normal stimuli they develop into connective tissue. Under other stimuli they develop into true epithelium. The transition from normal cells into epithelial cells can be definitely traced.

Aschheim-Zondek and Mazer-Hoffman Tests.—Bland and his associates state that the anterior pituitary hormone test of Aschheim and Zondek is a reliable laboratory adjuvant for the diagnosis of early pregnancy. In their hands it yielded 82.4 per cent correct positives and 93.2 per cent correct negatives. The finding of 6.8 per cent false positive results detracts somewhat from its complete reliability. Especially is this error likely to be encountered in women who are functionally sterile because of endocrine disturbances, or in women approaching the menopause. In these women, a compensatory hypertrophy of the anterior hypophysis may produce an excessive quantity of hormone, which, finding its way into the urine, will render an incorrect positive. The female sex hormone test of Mazer-Hoffman yields a smaller percentage of correct positives (76.3 per cent) but is somewhat more reliable in the positive diagnosis of pregnancy, especially in patients suffering with functional disturbances. A smaller percentage of false positives among nonpregnant patients was observed when this test was employed. This is probably due to the fact that hyperfunction of the ovaries, which would be necessary in order to produce an excess of female sex hormone in the urine and render a false positive, is rarely if ever found in cases of endocrine dysfunction. In those patients in whom there is a question of a dead fetus (missed abortion), the presence of a positive Aschheim-Zondek and a negative Mazer-Hoffman test, on repeated occasions, denotes that the fetus is probably dead. It appears that the female sex hormone disappears from the urine somewhat earlier than does the anterior pituitary hormone. Repeated negative Mazer-Hoffman tests in pregnancy in cases accompanied by slight bleeding denotes an insufficient quantity of female sex hormone and a threatened abortion. Only when the female sex hormone appears in demonstrable quantities in the urine may one feel assured that the ovum has secured a firm location and that the pregnancy may continue. The larger percentage of correct positives with the Aschheim-Zondek test, and the smaller percentage of false positives with the Mazer-Hoffman test, suggest that the two tests be simultaneously employed in every instance in order to yield the most accurate results.

Annals of Internal Medicine, Ann Arbor, Mich.

5: 825-954 (Jan.) 1932

*Quinidine Therapy in Treatment of Cardiac Irregularities Due to Hyperthyroidism. J. P. Anderson, Cleveland.—p. 825.
*Tachycardia. C. W. Barrier, Fort Worth, Texas.—p. 829.
Response of Cardiovascular System to Respiratory Strain: Measure of Myocardial Efficiency. A. Eustis, New Orleans.—p. 842.
Auricular Paroxysmal Tachycardia Caused by Digitalis: Report of Case. A. F. Heyl, New Rochelle, N. Y.—p. 858.
Medical and Surgical Problems Associated with Coronary Sclerosis. Arlie R. Barnes, Rochester, Minn.—p. 873.
*Pulmonary Infections by Friedländer's Bacillus (Bacillus Mucosus-Capsulatus). F. Fremmel, K. J. Henrichsen and H. C. Sweany, Chicago.—p. 886.
Syphilis of Lung: Report of Case with Autopsy Observations. H. C. Denman, Brooklyn.—p. 895.
Observations on Contour of Normal and Tuberculous Female Chests. S. A. Weisman, Minneapolis.—p. 907.
American Mountain Tick Fever: Semeiography and Nosology, with Remarks on Pathology and Treatment. N. Toomey, Palmyra, Mo.—p. 912.
Bilateral Double Kidney with Duplication of Ureters. R. M. Lintz, Brooklyn.—p. 924.

Quinidine in Treatment of Cardiac Irregularities Due to Hyperthyroidism.—Anderson reports that quinidine sulphate is a highly useful drug for the restoration of a normal cardiac rhythm if a thyroidectomy alone fails to achieve this result. Observations over several years show that the maximum benefit is obtained when the drug is given on the third or fourth postoperative day. A very few patients are sensitive to quinidine, thus prohibiting its use in such cases. By adding quinidine therapy after thyroidectomy when auricular fibrillation is still present, a normal cardiac rhythm will be restored in about 96 per cent of cases.

Tachycardia.—Barrier notes the important features in a series of twenty-six cases of supraventricular tachycardia. Cases of unusual duration are reported, one patient having an attack lasting three years, another being in a permanent attack for nearly six years unless treated. Quinidine in most cases of supraventricular tachycardia is the more desirable drug for arresting an attack, though in the presence of heart failure digitalis will act and may be the drug of choice. In two cases in which quinidine was continued for a year, it had to be used in increasing doses. Continuous digitalization has been extended over periods as long as one and a half years. While the continuous use of digitalis is to be preferred over quinidine, the drug must be used in such large doses that toxic effects appear. Both digitalis and quinidine will slow the rate and arrest the attacks in the same patient. Until the mechanism of these attacks is better known, the mode of action of drugs cannot be explained. Digitalis did not arrest an attack in a patient who had received 1/15 grain (0.004 Gm.) of atropine. Both digitalis

and quinidine act well by mouth, and few patients need the drugs by vein.

Pulmonary Infections by Friedländer's Bacillus.—Fremmel and his associates describe an extremely acute type of Friedländer's bacillus infection, the patient living only twenty-six hours from onset to death. The clinical signs corresponded to those usually reported for the disease. The pathologic changes were those of an uncommon lobar pneumonia instead of a confluent bronchopneumonia, or a "pseudo" lobar pneumonia. The disease began by a rapid growth of the encapsulated micro-organisms in the alveoli and smaller bronchi, causing an exudate rich in edema fluid containing scattered monocytes and irregularly placed fibrin, with an occasional hemorrhage into the alveoli. This aspect has only a gray to yellow-gray appearance grossly and accounts for the infrequent appearance of the red stage of hepatization. Death occurred before the other stages could develop. Ordinarily the evolution of the lesion from the "red" stage is characterized by an infiltration of polymorphonuclear leukocytes along the alveolar walls, forming in crescents along the plugs composed of bacilli, monocytes and varying amounts of fibrin. Later an invasion of the alveolar wall results in a huge dilatation of the alveolar capillaries, followed by thrombosis, necrosis and abscess formation. The last two processes correspond to the stage of resolution of pneumococcus pneumonia. The dilatation of the alveolar capillaries, with an occasional rupture into the alveoli, gives to the lesions a mottled dark red appearance that is occasionally present.

Archives of Ophthalmology, Chicago

7: 1-170 (Jan.) 1932

Blindness and Papilledema in Guernsey Calves, Usually Bulls, Including Results of Postmortem Examination of Two Affected Animals. G. E. de Schweinitz, Philadelphia.—p. 1.
*Mild Form of Epithelial Dystrophy of Cornea. S. R. Gifford, Chicago.—p. 18.
*Methods of Formation of Posterior Abscess in Ulcus Serpens. B. Samuels, New York.—p. 31.
Mechanism of Accommodation: Facts and Fancies. W. H. Luedde, St. Louis.—p. 40.
*Cataract of Postoperative Tetany: Report of Three Cases. C. S. O'Brien, Iowa City.—p. 71.
*Sympathetic Ophthalmia from Nonperforating Trauma: Report of Case. H. D. Lamb, St. Louis.—p. 97.
Unusual Retinal Vascular Changes in Traumatic Injury of Chest: Angiopathia Retinae Traumatica (Purtscher). W. H. Stokes, Omaha.—p. 101.
An Operative Procedure for Pyramidal Cataract. E. Selinger, Chicago.—p. 109.

Mild Form of Epithelial Dystrophy of Cornea.—According to Gifford, the mild form of epithelial dystrophy is distinguished by the presence of edema of the epithelium, numerous minute staining areas, reduced corneal sensitivity and, usually, low intra-ocular tension. It is not an uncommon condition and would undoubtedly be recognized more commonly if every patient complaining of a burning and scratching sensation with slightly reduced vision were examined with the slit lamp after staining with fluorescein. The use of ethylmorphine hydrochloride or phenacaine, or both, seems to exert a definitely favorable effect on the condition.

Formation of Posterior Abscess in Ulcus Serpens.—Samuels states that the majority of posterior abscesses in ulcus serpens are brought about by an aggregation of leukocytes derived from the deep ciliary vessels, traveling anterior to Descemet's membrane. Many, however, are formed by cells that have found their way forward into the cornea from the iris, through Descemet's membrane. It is probable that a considerable number of abscesses are derived from both sources.

Cataract of Postoperative Tetany.—O'Brien calls attention to the fact that rapidly developing bilateral cataracts in presenile persons, especially those of the female sex, may be due to postoperative tetany. In patients of this age one should always think of such a possibility. The diagnosis is made from (1) a history of thyroidectomy followed by spasms of the upper extremities and perhaps of other parts of the body, (2) a low blood serum calcium associated with a high blood phosphorus and (3) signs of hyperexcitability of the peripheral nervous system (Erb's, Chvostek's and Trousseau's signs). The forty-two reported cases of postoperative tetany with cataracts are discussed, and to these the author adds three typical cases. Cataracts develop with either manifest or latent tetany, and they advance despite treatment that may control all other manifestations. Probably there is no pathognomonic picture of this type of cataracta complicata, but it seems that the first changes appear as aggregations of fine opaque granules directly under the anterior and posterior capsules of the lens. The prognosis should be guarded because of the fact that delayed spontaneous hemorrhage may occur after lens extraction. Before and after such cataracts are extracted, the patient should receive parathyroid hormone, viosterol and a high calcium intake, in order that the blood and tissues may be in as nearly a normal state as possible.

Sympathetic Ophthalmia from Nonperforating Trauma.—Lamb reports a case of a child, aged 6 years, who suffered an abrasion of the cornea of the right eye from a blow with a stick. There was no penetrating wound. Ten weeks later the left eye showed involvement of the uveal tract, and the right eye was enucleated. In spite of intensive local and general treatment of various kinds, vision in the left eye was completely and hopelessly lost. Anatomic examination of the enucleated right eyeball revealed a definite sympathetic iritis and cyclitis. Fibrinoplastic exudate was small in amount; it formed some posterior synechial and pupillary membranes.

Archives of Pathology, Chicago

13: 1-192 (Jan.) 1932

*Early Lesions of Rheumatic Endocarditis. T. Leary, Boston.—p. 1.
*Functions of Glia in Secondary Degeneration of Spinal Cord. F. Cramer, New York, and B. J. Alpers, Philadelphia.—p. 23.
Chloro-Erythroblastoma: Report of Case. N. J. Howard and J. B. McNaught, San Francisco.—p. 56.
*Pathogenesis of Bronchiolitis Obliterans: Observations in Cases of Bright's Disease. W. Ehrich and J. F. McIntosh, New York.—p. 69.
Encephalitis of Dogs with Eck Fistula Fed on Meat. J. Baló and B. Korpássy, Szeged, Hungary.—p. 80.
Hemochromatosis and Primary Carcinoma of Liver: Report of Case, with Review of Literature and Discussion of Pathogenesis. S. R. Rosenthal, Chicago.—p. 88.
Coagulofloccculation Test for Malignant Tumors. E. Weiss, Chicago.—p. 106.

Early Lesions of Rheumatic Endocarditis.—Leary describes the early lesions of rheumatic endocarditis. The characteristic lesion consists in the formation of a defensive palisade of cells on the contact edges of the valves. Three phases of this reaction are illustrated: one before verruca formation with bacteria on the surface of the palisade; one showing verrucae without demonstrable organisms; one with mucoid (?) degeneration of the palisade in an old, scarred valve, without organisms, and showing pseudoverruca formation due to bland thrombosis. The evolution of the verrucae from local regions of damage of the defensive palisade is described.

Functions of Glia in Secondary Degeneration of Spinal Cord.—Cramer and Alpers made a study of experimental secondary degeneration of the fibers of the spinal cord in rabbits, with the use of the metallic impregnation methods of the Spanish school, the aim being to study the three types of glia in this reaction. The degenerative reactions were studied in various representative stages up to and including the seventy-eighth postoperative day. The study revealed and confirmed the fact that the glial cells, both ectodermal and mesodermal, were the active agents in the phagocytosis of the degenerated nerve fibers. The oligodendroglia were shown to be the first active glial cells in the phagocytosis of the effete nerve fibers. In conjunction with a belated activity on the part of the microglia, the oligodendroglia were shown to continue their phagocytic activities until the axomyeline material had been fermented into true fat. The substantiation of the fact of active phagocytosis on the part of the oligodendroglia, accompanied by that of the microglia, was made on the basis of distinctly different cyto-architectonic qualities in the phagocytic derivatives of these two types of cells. The phagocytic digestive activity of the ectodermal types, i. e., the oligodendroglia, is compared to that of glandular cells. The astrocytes were shown to have a particularly sturdy reaction during the earlier weeks of the degenerative process, with some exceptions, but in the later weeks to engulf fat and the other products of the degenerated nerve fibers. A hyperplasia on the part of the ectodermal glia, leading to the formation of new oligodendroglia and macroglia presumably for the purposes of the ultimate digestion and disposition of the fat, was demonstrated. The last function of the macroglia was seen to be in the nature of cicatrix formation in the areas of degeneration.

Pathogenesis of Bronchiolitis Obliterans.—In the postmortem examination of certain cases of Bright's disease in which uremia was present at the time of death, Ehrich and McIntosh observed fresh pneumonic areas besides extensive lesions of preexisting obliterative bronchiolitis. They believe that cases of obliterative bronchiolitis described heretofore are divisible in two groups depending on their etiology and pathogenesis. The severe destruction of the bronchial walls seen in them was missing in the third group, which the authors describe for the first time. Absorption of the exudate failed in this group because of the disturbance of metabolism which often occurs in the uremia of Bright's disease and which manifests itself by increased tendency to exudation and decreased tendency to absorption. In two cases, at least, the occurrence of bronchiolitis was caused by bacterial infection. Whether it can arise as the result of intoxication alone, as does general serositis, could not be decided.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

13: 1-64 (Jan.) 1932

*Influence of Ultraviolet Rays on Pharmacologic Potency of Digitalis. D. I. Macht, Baltimore.—p. 5.
Therapeutic Effects of Physical Exercise. R. L. Johnston, Cleveland.—p. 15.
Importance of Static Massage Following Diathermy. J. E. Rueth, Milwaukee.—p. 21.
Established Actinotherapeutic Modalities in Dermatology. M. Scholtz, Los Angeles.—p. 28.

Influence of Ultraviolet Rays on Potency of Digitalis.—Macht irradiated tincture of digitalis with mercury vapor quartz lamps, with roentgen rays and with radium. He noted that irradiation with ultraviolet rays for short periods produces a deterioration or weakening in the pharmacologic potency of the tincture, as tested on living plants and animals. On progressive and prolonged exposure to ultraviolet rays, a point is reached when the photochemical changes result in the formation of products exhibiting a greater toxicity for both plants and animals. This stage, on still further exposure, is followed by a secondary weakening in the pharmacologic potency of the irradiated tincture. The shorter ultraviolet rays, particularly those transmitted through a chlorine-bromine gas filter, are more effective than the longer rays in producing the changes described. Exposure to roentgen rays, to radium and to radium emanations results in a product which is greatly reduced in its activity for the animal heart, on the one hand, but is greatly increased in toxicity for living plant protoplasm, on the other.

Delaware State Medical Journal, Wilmington

3: 217-248 (Dec.) 1931

Shall the Profession Undertake Control of Specialization in Medicine? H. O. Reik, Atlantic City, N. J.—p. 217.

Journal of Experimental Medicine, Baltimore

55: 169-323 (Feb.) 1932

*Immunologic Reactions of Pneumonic Pleural Fluids. M. Finland, Boston.—p. 169.
Toxin-Antitoxin Reaction Without Neutralization. J. Freund, Philadelphia.—p. 181.
*Note on Specific Agglutination of Pneumococcus Types I, II and III. J. F. Enders, Boston.—p. 191.
Relation of Hydrostatic Pressure to Gradient of Capillary Permeability. P. D. McMaster, S. Hudack and P. Rous, Baltimore.—p. 203.
*Studies on Influenzal Meningitis: I. Problems of Specific Therapy. H. K. Ward and Joyce Wright, Boston.—p. 223.
Id.: II. Bacillus Influenzae: Problem of Virulence and Resistance. Joyce Wright and H. K. Ward, Boston.—p. 235.
*Incidence of Cancer in Tarred and Sheltered Mice. P. Rous and Elizabeth Botsford, Baltimore.—p. 247.
Antigenic Streptococcal Hemolysin. E. W. Todd, Surrey, England.—p. 267.
Nutritional Requirements in Vitro of Normal and Malignant Mouse Epitheliums. L. Santesson, Baltimore.—p. 281.
Experimental Nephritis in Frog: IV. Significance of Functional Response to Vascular and Parenchymal Disturbances in Kidney. Jean Oliver, Brooklyn.—p. 295.
Multiplication of Virus of Mexican Typhus Fever in Fleas. H. Mooser and M. R. Castaneda, Boston.—p. 307.

Immunologic Reactions of Pneumonic Pleural Fluids.—Finland studied thirty-one pleural fluids from nineteen patients with typical lobar pneumonia, and four fluids from three patients with other diseases for controls. He found that pleuritic exudates from patients with lobar pneumonia may be sterile or infected. Sterile fluids, at or about the time of crisis, contain actively acquired antibodies similar to those in the blood serum. Infected fluids do not contain such antibodies, presumably because of the presence in them of large amounts of soluble specific substance. Sterile fluids from patients treated with immune serums have both horse serum and antibodies similar to those injected. Infected fluids from serum-treated cases contain horse serum and such heterologous antibodies as were contained in the therapeutic serums together with homologous soluble specific substance. The concentration of horse serum and antibodies in pneumonic fluids is usually the same as or somewhat less than that of the corresponding blood serums.

Specific Agglutination of Pneumococcus Types I, II and III.—Enders demonstrated type-specific agglutination of pneumococcus types I, II and III in antiserums largely deprived of the carbohydrate antibody. The type-specific agglutinogens in pneumococcus I and II responsible for agglutination in such antiserums are inactivated by heating in alkaline solution at 100 C. The specific carbohydrate remains unaltered under these conditions. The relationship of the type-specific agglutinogen in pneumococcus I to the type-specific A substance has been discussed. The possible application of these results to the standardization of therapeutic antiserums by agglutinin titer has been discussed. On the basis of experiments performed, a tentative explanation is offered for the failure of pneumococcus type II to absorb the agglutinins from anti-Bacillus friedlaenderi type B serum.

Influenzal Meningitis.—According to Ward and Wright, an acute purulent meningitis due to the invasion of the meninges by Pfeiffer's influenza bacillus is not a very uncommon disease in infants and young children. It has a very high mortality. Complement is entirely absent in the cerebrospinal fluid of these cases, and bactericidal experiments suggest that the injection of a specific antiserum will have but slight lethal effect on the organisms unless complement is injected at the same time. Treatment with a mixture of specific antiserum and complement led in some cases to a definite clinical improvement, coincident with sterilization and clearing of the cerebrospinal fluid. But after some days the patients relapsed and died. Necropsy showed localized abscesses in the vicinity of the base of the brain, the lesions being definitely walled off from the general subarachnoid space. One patient recovered. Since the walls of the abscesses apparently present an insuperable mechanical obstacle to the action of the antiserum and complement, the possibility of preventing the formation of abscesses is discussed. Earlier diagnosis and more rapid sterilization are the most obvious measures. Bactericidal experiments indicate that the proportion of antiserum to complement may be an important factor in bringing about a more rapid elimination of the bacilli.

Cancer in Tarred and Sheltered Mice.—Rous and Botsford report that mice sheltered for long periods from the intercurrent access of living entities out of the environment developed tar cancer with the same frequency as controls exposed to an unusual extent. This happened although the food of the two groups differed profoundly in character.

Journal of Immunology, Baltimore

22: 1-74 (Jan.) 1932

*Study of Action of Saliva and Extract of Tonsils on Diphtheria Bacillus and Diphtheria Toxin. I. Bézi, Rochester, N. Y.—p. 1.
*Complement Binding Properties of Brucella Abortus of Bovine and Porcine Origin. S. T. Walton, Detroit.—p. 19.
Age and Susceptibility of Rabbits to Scarlet Fever Toxin. J. D. Trask, New Haven, Conn.—p. 41.
Method for Agglutination of Hemolytic Streptococci. J. H. Mueller and Katharine S. Klise, Boston.—p. 53.
Studies on Adsorption of Diphtheria Toxin to and Elution from Magnesium Hydroxide. E. E. Ecker and L. A. Weed, Cleveland.—p. 61.
Study of Antigenic Activity of Preparations Made from Various Strains of Treponema Pallidum. Christine E. Rice, Albany, N. Y.—p. 67.

Action of Saliva and Extract of Tonsils on Diphtheria Toxin.—Bézi records the results of experimental tests of the action of saliva and extracts of tonsils and other organs on diphtheria toxin. Evidence is presented which seems to indicate that some specimens of saliva may exert an antibacterial action against diphtheria bacilli and that saline extracts of tonsils and lymph nodes may inhibit the necrotizing action of diphtheria toxin. It has not been determined whether or not these reactions are specific, and the experiments do not permit the drawing of definite conclusions.

Complement Binding Properties of Brucella Abortus.—Walton reports experiments which indicate that complement fixation as a means of detecting Bacillus abortus antibody is on a par with the more widely used method of agglutination. No particular advantage can be claimed for it over agglutination, but, as is the case with any serologic test when the laboratory report conflicts with the clinical evidence, or when clinical signs are wanting as is often the case in dealing with these organisms, an additional test, detecting a different type of antibody, might often be advisable as a confirmatory measure.

Journal of Nutrition, Springfield, Ill.

5: 1-101 (Jan.) 1932

*Mineral Exchanges of Man: II. Effect of Excess Potassium and of Calcium on Two Normal Men and on an Edematous Nephritic. S. H. Bassett, E. A. Elden and W. S. McCann, Rochester, N. Y.—p. 1.
*Effect of Vitamin Withdrawal on Monkey (Macacus Rhesus). R. G. Turner and E. R. Loew, Detroit.—p. 29.
Hemoglobin Content of Blood of Dairy Cattle. H. J. Brooks and J. S. Hughes, Manhattan, Kan.—p. 35.
Factors Which Determine Concentration of Calcium and Inorganic Phosphorus in Blood Serum of Rats: Second Paper. B. Kramer and J. Howland, Baltimore.—p. 39.
Technic for Studying Lactation in Small Animals and Its Use in Evaluating Protein Levels in Diet. Marja Kozlowska, C. M. McCay and L. A. Maynard, New York.—p. 61.
*Protein Intake and Basal Metabolism of College Women. Rossleene A. Hetler, with assistance of Marie Killinger and Margaret Plant, Urbana, Ill.—p. 69.
*Variations in Blood Sugar Values of Normal and Vagotomized Dogs Following Glucose Administration. J. P. Quigley, W. R. Hallaran and B. O. Barnes, Cleveland.—p. 77.

Mineral Exchanges of Man.—Bassett and his associates report that potassium citrate when added in quantities of 7.8, 10.5 and 24 Gm., respectively, to the diets of two normal men and to the diet of a patient with nephritis and edema, for periods of five days in each instance, did not alter the metabolism of calcium, magnesium or phosphorus. The ingestion of 9.8 and 13 Gm. of calcium chloride per diem by the normal men for five-day periods led to marked increase in the urinary and fecal calcium excretion and at least temporarily to positive calcium balances. In the nephritic subject in whom the ingestion of 2.2 Gm. per diem of calcium chloride was accompanied by intramuscular injection of large doses of parathyroid extract, urinary calcium excretion was increased but the quantity excreted was much less than that excreted by the normal men during the control period. Fecal calcium in his case was excessive and resulted in a distinctly negative calcium balance. The magnesium balances of all three subjects became negative during the period of calcium chloride-parathyroid extract administration. The influence of calcium chloride feeding on phosphorus metabolism could not be completely evaluated because of the number of variable factors entering into the experiment. High potassium feeding for five-day periods did not produce negative balances in the metabolism of sodium and chlorine in the normal subjects. The much larger doses of potassium citrate taken by the nephritic subject caused a marked increase in the urinary excretion of sodium and chlorine, which resulted in negative balances for both elements. Diuresis, sweating and weight loss accompanied the increased excretion of sodium and chlorine. In the normal subjects, sodium and potassium balances were negative during the period of calcium feeding. This is believed to have been due to the acid effect of calcium chloride, but the negative potassium balances may have been due to delay in excretion of this element resulting from administration of potassium citrate in the immediately preceding period. The comparatively small doses of calcium chloride given the man with nephritis did not affect his sodium or potassium metabolism. Attention is called to the unusually small amount of sodium and calcium excreted in the urine of the nephritic subject during the control period, and this is contrasted with his normal urinary excretion of potassium and magnesium. The total nitrogen metabolism was not affected by the administration of potassium citrate or calcium chloride. Iron was stored by both normal subjects on an average food iron intake of 21 mg. per diem. In the nephritic subject, if one excludes the control period, a food iron intake of 12 mg. per diem was sufficient to maintain iron balance.

Effect of Vitamin Withdrawal on Monkey.—Turner and Loew describe experiments which indicate that withdrawal of vitamin A from the monkey does not develop a characteristic susceptibility toward infections of the upper respiratory tract. Xerophthalmia, at least, is difficult to produce and no definite changes in the tissues of the upper digestive tract are observed. Thus it seems that infection of the upper respiratory tract brought about by experimental diets are encountered most frequently when that portion of the tract is affected by a change in cell structure.

Protein Intake and Basal Metabolism of College Women.—Hetler conducted a study of the urinary nitrogen excretion, basal metabolism, and food intake of eighty-five college women for the purpose of determining the habits of protein consumption in women and the possible interrelationship between protein intake and basal metabolic rate. The average daily protein intake of the group studied was 0.94 Gm. per kilogram of body weight, a value slightly lower than the daily protein ingestion characteristic of male medical students as determined by Denis and Borgstrom, by Beard and by Brooks. The average twenty-four hour urinary nitrogen excretion for the group was 7.69 Gm. The average basal metabolism for the group was found to be lower than the standard. The deviation of the actual basal metabolism from the Harris-Benedict standard averaged —7.1 per cent. There appeared to be no definite interrelationship, within the group, between protein intake and basal metabolic rate. It is suggested that the lower protein intake of women may be in part responsible for the fact that their basal metabolic rate is usually lower than that of men.

Blood Sugar of Normal and of Vagotomized Dogs.—Quigley and his associates propose a method by which a determination of the rate at which dextrose is removed from the circulation following the administration of dextrose would give information regarding the ability of the animal to metabolize sugar. This method has been employed on normal and on doubly vagotomized dogs. Curves showing composite results are presented. If dextrose is administered twenty hours preceding the test, an increase in the ability to metabolize sugar is noted in vagotomized but not in normal animals. Chronic vagotomy does not reduce the sensitivity of the mechanism that is stimulated by the administration of dextrose; the mechanism rather appears to be slightly more irritable. If these results are to be interpreted as indicating the rate of insulin secretion, they tend to show that hyperglycemia will lead to at least as great a secretion of insulin in the pancreas freed from central vagus control as in the normal islet tissue.

Journal of Urology, Baltimore

27: 1-127 (Jan.) 1932

*Tumors of Adrenal Gland: Report of Two Cases of Paraganglioma of Adrenal Gland. J. A. Lazarus and A. A. Eisenberg, New York.—p. 1.
Malignant Leiomyoma of Kidney. A. H. Crosbie and H. Pinkerton, Boston.—p. 27.
*Rare Renal Tumors. L. C. Jacobs and L. H. Hoffman, San Francisco.—p. 33.
Adenocarcinoma Horseshoe Kidney. E. Hess, Erie, Pa.—p. 47.
*Division of Horseshoe Kidney for Relief of Ureteropelvic Junction Obstruction. P. F. Donohue, St. Paul.—p. 59.
*Acute Hemorrhagic Cyst of Kidney. A. D. Munger, Lincoln, Neb.—p. 73.
Traumatic Lesions of Urogenital Tract. C. M. McKenna, Chicago.—p. 95.
Differential Diagnosis of Pathologic Conditions of Urinary Tract and Female Generative Organs. W. E. Stevens, San Francisco.—p. 103.
New Surface Anesthetic in Urology. H. W. E. Walther, New Orleans.—p. 119.
New Kidney Clamp. N. F. Ockerblad, Kansas City, Mo.—p. 125.
Skiodan Pictures. W. B. Dakin, Los Angeles.—p. 127.

Suprarenal Tumors.—Lazarus and Eisenberg classify and describe suprarenal tumors as indicated by a general survey of the literature. Such tumors are rare. The most important growths from a clinical and pathologic point of view are those arising from the epithelial component of the gland. The noteworthy features of the tumors involving the suprarenal cortex are the associated sex changes, which have been designated as the suprarenal-genital syndrome, most frequently seen in female children. As a result of the fact that the suprarenal medulla is an offshoot of the sympathetic nervous system, tumors arising from this part of the gland bear a close resemblance to tumors of the sympathetic system; and the degree of malignancy shown by these new growths varies inversely with the state of maturity of the medullary cells. The more mature the cells, the more benign the growth. Paraganglioma is a tumor composed entirely of mature chromaffin cells of the suprarenal medulla,

is usually benign and, unlike all other suprarenal tumors, occurs only in adults. Suprarenal tumors have a tendency to cause irreducible renal ptosis. Fever and skin pigmentation are suggestive symptoms. The finding of a large ovoid shadow in the roentgen plate situated over a ptosed and rotated kidney is suggestive of a suprarenal tumor. The authors present two cases of paragangliomas both in women 58 years of age, in one of which the roentgenograms led to a tentative diagnosis of a suprarenal cyst, while in the other the presence of the paraganglioma was clinically overshadowed by the coexisting carcinoma of the thyroid and not discovered till necropsy. A review of the literature seems to show that the second case is the only one on record of a paraganglioma metastasizing in other organs and thereby indicating that this tumor possesses potentially malignant properties.

Rare Renal Tumors.—According to Jacobs and Hoffman, a tumor invading the retroperitoneal perirenal fossa when of the mixed cell sarcoma type is of the highest degree of malignancy. Myxomas, while only locally recurrent, are equally grave as to prognosis. The treatment should be surgical and should consist in the complete removal of kidney and tumor mass, including the adipose capsule. The perirenal fat should likewise be dissected from the peritoneum and from the muscles of the posterior abdominal wall. The application of radium and high voltage roentgen therapy at the site of the nephrectomized area should be immediately instituted. The prognosis is extremely grave, the expectancy of life being less than one year. Recurrences at the original site are common and are immediately followed by generalized metastases.

Division of Horseshoe Kidney.—In cases of horseshoe kidney, Donohue recommends division of the isthmus for the relief of upper urinary tract obstruction when advanced changes have not occurred in either kidney. Division of the isthmus separates the two kidneys. This allows free movement of the affected kidney and permits the reconstruction of the upper urinary tract. The kidney is rotated until the pelvis and ureter are in their normal position medial to the renal mass. Nephropexy is performed and the kidney is fixed in position as high as possible in the renal fossa with the upper pole close to the vertebral column and the lower pole swung outward to restore the normal vertical axis and prevent angulation at the ureteropelvic junction. This position permits normal kidney function. In some cases, division of aberrant vessels crossing the ureteropelvic junction will be necessary. Pain may arise in the opposite kidney following division of the isthmus. This is probably due to a loss of the support of the isthmus and further descent of the second kidney, causing some degree of obstruction. In this event, operation on this kidney with correction of the malposition and nephropexy are indicated.

Acute Hemorrhagic Cyst of Kidney.—Munger presents the clinical and histologic study of what undoubtedly was a symptomless solitary renal cyst. It was filled with something other than blood for an indefinite period but led to an acute condition by becoming hemorrhagic. Through this transition period it developed from a symptomless lesion to one of a definite hemorrhagic nature with violent symptoms, and the gross and histologic changes corresponded basically with those described for the so-called hemorrhagic cysts of the kidney. On the basis of this study the author considers that the term "hemorrhagic cyst" is a misnomer. Such lesions of the kidney are occasioned by a hemorrhage into a cyst of varied origin and should be grouped in accordance with the histogenesis. In this case it is a cyst of lymphogenic origin with hemorrhage. These cysts are relatively rare and present no characteristic symptom complex. Treatment is surgical: resection, when possible; otherwise, nephrectomy.

Medical Journal and Record, New York

135: 53-104 (Jan. 20) 1932

Immunotherapy in Its Nonspecific Phases. E. Bonime, New York.—p. 53.
Coronary Artery Disease. M. S. Jacobs, Philadelphia.—p. 58.
Fatal Coronary Occlusion Following an Injection of Local Anesthetic. E. Weiss, Philadelphia.—p. 61.
Modern Conception of Deafness. H. Hays, New York.—p. 62.
Acute Upper Respiratory Infection in Infants and Children. S. A. Cohen, New York.—p. 64.
Occurrence and Significance of Leukopenia: Review of Recent Literature. C. W. Mucklé, Philadelphia.—p. 68.

Minnesota Medicine, St. Paul

15: 73-140 (Feb.) 1932

*Lumbar Anesthesia: Résumé of Seven Hundred and Fifty-One Cases. W. C. Stillwell, Mankato.—p. 73.
*Achlorhydria and Hypochlorhydria in Peptic Ulcer. J. A. Wilson and G. Earl, St. Paul.—p. 79.
Peptic Ulcer: Review of Recent Opinions of Etiology and Treatment. A. M. Snell, Rochester.—p. 86.
Convulsions in Childhood. M. G. Peterman, Milwaukee.—p. 91.
Normal and Abnormal Motility Syndromes of Upper Urinary Tract, with Indications for Drug and Sympathectomy Therapy. W. P. Herbst, Minneapolis.—p. 93.
Conservation of Hearing. J. T. Schlesselman, Mankato.—p. 95.
Injection Treatment of Hemorrhoids: Fallacies and Complications. W. A. Fansler, Minneapolis.—p. 98.
Seventeenth Century Pediatrics: An Anthology. O. W. Rowe, Duluth.—p. 101.

Lumbar Anesthesia.—On the basis of his observations in 751 cases, Stillwell believes that lumbar anesthesia in competent hands is the safest and most satisfactory of all forms of anesthesia. Any surgeon who once becomes familiar with its ease of administration and its advantages both to the patient and to himself will never want to go back to other methods. The complete relaxation of the muscles (which is found only in the deep stages of ether anesthesia) and the quiet abdomen facilitate rapid and thorough surgery. During the anesthesia it is found that active intestinal peristalsis is present and that the kidneys show an increased urinary secretion. Postoperative complications are fewer and much less severe than with inhalation anesthesia. The lack of postoperative vomiting and abdominal distention reduces nursing care to a minimum. With the advent of newer technics, it is possible that a more localized and longer anesthesia may be available in the near future.

Achlorhydria and Hypochlorhydria in Peptic Ulcer.—According to Wilson and Earl, an active peptic ulcer in the presence of true gastric achlorhydria is so rare as to be negligible. Histamine stimulation of gastric secretion should always be tried before diagnosing achlorhydria, or even hypochlorhydria, when peptic ulcer is suspected. In the authors' experience it has caused free acid to appear frequently when the ordinary test meals showed achlorhydria. Aspirations of the stomach at the time of suspected ulcer distress, or four hours after a heavy meal or Riegel meal, should be resorted to if an Ewald meal shows no free acid. Failure to use all these useful procedures is responsible for nearly all the reported and erroneous diagnoses of achlorhydria associated with peptic ulcer.

New England Journal of Medicine, Boston

205: 1223-1272 (Dec. 24) 1931

Tumors and Near Tumors of Bone. F. J. Cotton, Boston.—p. 1223.
*Etiologic Factors in Hypertension. R. S. Palmer, Boston.—p. 1233.
*Involvement of Central Nervous System in a Case of Glandular Fever. S. H. Epstein and W. Dameshek, Boston.—p. 1238.
Review of Observations of Committee on Medical Care, White House Conference, February, 1931. R. B. Osgood, Boston.—p. 1241.
*Neurologic Phenomena in Course of Treatment of Diabetes. M. Criscitiello, Jr., and E. R. Messer, Pittsfield, Mass.—p. 1246.
Mistakes in Diagnosis and Treatment of Syphilis. A. W. Cheever and W. D. Wheeler, Boston.—p. 1249.

Etiologic Factors in Hypertension.—Palmer believes that the two chief etiologic factors in hypertension are an inherited predisposition and obesity. There may be many contributory factors such as dietary errors, endocrine dysfunction, diminished chest volume, foci of infection, allergy and nervous strain, which may prove important in individual cases but which are not generally significant. The practical indications are to recognize the potential hypertensive patient from his family history, to guard him against obesity and to consider whether any of the contributory factors of hypertension exist in that particular individual.

Involvement of Central Nervous System in Glandular Fever.—Epstein and Dameshek report a case of glandular fever (infectious mononucleosis) with striking cerebral symptoms. In this case there was demonstrated a parallelism between the cells of the spinal fluid and the white blood cells. The authors consider it probable that the central nervous system symptomatology in this case was part of the general systemic disease.

Neurologic Phenomena in Treatment of Diabetes.—Criscitiello and Messer present a case of diabetic coma which, in the course of treatment, showed rare neurologic signs due to

hyperinsulinism. The mechanism of dextrose metabolism is briefly reviewed and the importance of afternoon blood sugar estimations is emphasized. If at any time during the treatment of diabetes any unusual symptoms or signs develop, it is important to have a blood sugar estimation.

206: 103-150 (Jan. 21) 1932

*Study of One Hundred and Two Cases of Atrophic Arthritis: I. Introduction: Statistical Data. M. Smith, Boston.—p. 103.
*Treatment of Pilonidal Sinus and End-Results. R. B. Cattell, Boston, and L. W. Stoller, Pittsfield, Mass.—p. 110.
Bacteriologic Point of View. R. L. Cecil, New York.—p. 114.
*Therapeutic Use of Sterile Mineral Oil in Bladder. B. E. Greenberg and M. L. Brodny, Boston.—p. 122.
Convenient Technic for Steam Inhalations for Bed Patients. J. H. Means and J. Lerman, Boston.—p. 124.

Atrophic Arthritis.—Smith presents a classification of atrophic arthritis which he believes may help to correlate some of its variable features. Preliminary evidence is produced which indicates that the members of this classification are different manifestations of the same disease. The author hopes that his presentation may help to engender a spirit of discontent with present concepts of the disease. Two papers that are to follow will deal with additional and more important clinical evidence against too narrow and simple ideas of its etiology and mechanism.

Treatment of Pilonidal Sinus.—Cattell and Stoller report the cases of fifty-nine patients with pilonidal sinus, together with the end-results of treatment in forty. They believe that operation should consist of complete excision of a block of skin and fat together with all the sinus tract. In their experience, the utilization of a large pedicle flap to fill the defect has reduced the number of recurrences and reduced the time of healing.

Therapeutic Use of Sterile Liquid Petrolatum in Bladder.—According to Greenberg and Brodny, liquid petrolatum has a palliative effect on the bladder, mechanically relieving the symptoms of various types of inflammation. It is an ideal medium for increasing the capacity of the bladder by distention. The after-effects of cystoscopic procedure on the bladder are alleviated by oil instillations. The incrustations, in cases of alkaline incrusted cystitis, are removed and floated off easily by oil. Oil has a hemostatic tendency. Some of the oil is retained in the normal bladder for from five to seven days.

South Carolina Medical Assn. Journal, Greenville

28: 1-24 (Jan.) 1932

Experience with Spinal Anesthesia. G. H. Bunch, Columbia.—p. 3.
Clinical Appraisal of Spinal Anesthesia. J. R. Young, Anderson.—p. 6.
Some Medical Aspects of Prostatic Surgery. G. R. Wilkinson, Greenville.—p. 11.
Strictures and Kinks of Ureter. W. R. Barron, Columbia.—p. 15.

Southwestern Medicine, Phoenix, Ariz.

16: 1-48 (Jan.) 1932

*Problems and Management of Intractable Asthma. G. Piness and H. Miller, Los Angeles.—p. 1.
Headaches Due to Specific Hypersensitiveness: History Taking and Etiology. R. M. Balyeat and H. J. Rinkel, Oklahoma City.—p. 5.
Gastro-Intestinal Allergy and Its Sequelae. V. G. Presson and R. A. Wilson, Tucson, Ariz.—p. 8.
Cicatricial Stricture of Esophagus. S. A. Schuster and F. P. Schuster, El Paso, Texas.—p. 14.
Chorea Gravidarum: Case Report. W. A. Guynes, El Paso, Texas.—p. 15.
Hypertension: Etiology and Prognostic Tests. E. W. Rheinheimer, El Paso, Texas.—p. 17.
Intestinal Obstruction. F. P. Miller, El Paso, Texas.—p. 20.
Epidemiology of Cerebrospinal Fever. R. J. Stroud, Tempe, Ariz.—p. 22.
Our Society (Presidential Address). E. P. Palmer, Phoenix, Ariz.—p. 23.
Ethics of Consultation. H. B. Gudgel, Phoenix, Ariz.—p. 25.
Ethical Relations Among Doctors. M. I. Leff, Glendale, Ariz.—p. 26.
Osteomyelitis. J. L. Borah, Phoenix, Ariz.—p. 27.
Public Health Laboratory Service. M. Greenfield, Santa Fe, N. M.—p. 29.
Rotary and the Crippled Child. J. M. Greer, Phoenix, Ariz.—p. 30.
Case Report. S. D. Swope, El Paso, Texas.—p. 33.
Electrocautery in Tuberculosis of Larynx. D. R. Gaskins, Phoenix, Ariz.—p. 34.
Public Health Notes. J. R. Earp, Santa Fe, N. M.—p. 35.

Problems and Management of Intractable Asthma.—According to Piness and Miller, there is one phase of the treatment of the intractable asthmatic patient which must be given especial attention and that is the acute, prolonged and ungovernable attack of asthma. These attacks are of the type that not infrequently precede a fatal outcome. In the rôle of allergist, the authors have had occasion to see a considerable number of patients in such paroxysms and what they have to say with regard to their care is the result of their experience with them. They see the patients late in the attack, after epinephrine has been used to the point at which it is no longer effective, after cyanosis of marked degree has set in and has been relieved by the administration of oxygen, when repeated use of any one of a number of narcotics (such as morphine, codeine or pantopon) has been made, all without avail. The patient is usually semiconscious, cyanotic, desiccated, and suffering from agonizing, exhausting dyspnea. To handle these patients without hospitalization is inviting disaster. They should be placed in a hospital, preferably in a room especially prepared to eliminate all environmental factors that are possible causative agents in precipitating or prolonging an attack. Fluids are forced by rectum, intravenously or by hypodermoclysis. Sedatives, such as chloral, bromides or chlorbutanol, by rectum, are often effective in quieting the nervous irritability of patients. Instead of oxygen, carbogen is used to stimulate deeper respiration, thus often opening up bronchi occluded by mucus plugs. Removal of such plugs can also be facilitated by the intravenous administration of sodium iodide. Caffeine hypodermically has proved of great value in supporting the circulatory system of such patients, and at times has proved a successful substitute for epinephrine.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

40: 53-104 (Feb.) 1932

Carcinoma of Breast: Critical Study of Twenty-Five Cases. C. D. Lockwood, Pasadena, Calif.—p. 53.
*Pain of Tumors of Spinal Cord. W. M. Craig, Rochester, Minn.—p. 56.
*Necrosis of Gallbladder. E. S. Judd and H. K. Gray, Rochester, Minn.—p. 64.
Calcification of Gallbladder. R. Brown, Santa Barbara, Calif.—p. 70.
Chemical Aspects of Acute Intestinal Obstruction. T. G. Orr, Kansas City, Kan.—p. 72.
Treatment of Acute Generalizing Peritonitis. L. F. Barney, Kansas City, Kan.—p. 76.
Comparative Relationship of Postoperative Gastric and Intestinal Hemorrhages to Postoperative Pulmonary Embolism. J. E. Summers, Omaha.—p. 83.

Pain of Tumors of Spinal Cord.—Craig believes that the history of pain is probably one of the noteworthy features in summing up the differential diagnosis between tumors of the spinal cord and lesions elsewhere in the body which produce similar symptoms. In a large percentage of cases, the symptom of pain is associated with some motor or sensory derangement which immediately gives a clue as to the nature of the underlying pathologic process. However, there are some cases of tumor of the spinal cord in which pain persists as the chief symptom for a number of months, or even years, proving so resistant to the more conservative forms of treatment that more radical measures seem imperative and, in the apparent absence of associated neurologic symptoms, operations on the abdomen or other regions are often carried out in the mistaken hope of relieving this pain. In reviewing a large series of cases of tumor of the spinal cord, the author found that such surgical procedures had been carried out in more than 10 per cent of the cases. Examples of these cases are presented in an effort to emphasize that, if the type of pain suggests that it may be of central origin, it is necessary to analyze the pain and to make repeated neurologic and other examinations, even in the presence of other coexisting pathologic changes.

Necrosis of Gallbladder.—According to Judd and Gray, necrotic lesions in the gallbladder are being observed with increasing frequency. Among members of the medical profession a rather high incidence may be noted. This may be attributed to the rather general disinclination on the part of physicians to seek medical attention until symptoms have become so unbearable that they cannot procrastinate further. The exact etiology of this condition is not known. Undoubtedly a combination of factors is responsible, and if it is possible to eliminate any or all of the probable underlying contributing agents, this should be accomplished with exacting thoroughness. Included in this program of prophylaxis is the elimina-

tion of all foci of infection. The removal of gallbladders containing calculi should be advised if the patient's general condition warrants. The presence of stones is sufficient evidence of inflammation to consider cholecystectomy. The majority of patients have suffered from repeated attacks which, in most instances, are undoubtedly biliary colics caused by stone. Early diagnosis and proper surgical procedures at the time will obviate much suffering and correct the condition before it advances to the stage at which death of tissue has occurred.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Bristol Medico-Chirurgical Journal, London

48: 233-303 (Winter) 1931

The Partnership Between Anesthesia and Surgery. A. L. Flemming.—p. 233.
Silicosis: I. Administrative and Clinical. J. A. Nixon.—p. 253.
*Silicosis: II. Radiology and Pathology. G. B. Bush.—p. 259.
Congenital Abnormalities of External Ear. E. Watson-Williams,—p. 273.
Hematuria in the Preeruptive Stage of Measles. F. G. Jenkins.—p. 275.
*Cyanosis in Fatal Bronchopneumonia of Influenza. F. E. Fletcher.—p. 277.

Silicosis: Radiology and Pathology.—Bush states that the typical results of the inhalation of finely divided silica dust over long periods of time, or in strong concentrations, is first to produce what may be called a chronic lymphatic congestion, with possibly some bronchiolitis, a stage from which recovery may be expected with little or no disability or fibrosis; then to produce the simple nodular "dust fibrosis" which is silicosis; and, finally, in most cases to lead on to a condition of "infective silicosis" and to a true "dust phthisis." Individual cases show many variations in character and mode of development, depending on the factors of time, intensity and infection, and on the nature of the dust inhaled. Pathologic changes in the lymph nodes previously affected in early life by tuberculosis and other agencies, together with the initial physique and the degree of inherited or acquired resistance to infection, all have an influence on the rapidity of onset and progression of the disease.

Cyanosis in Fatal Bronchopneumonia of Influenza.—Fletcher presents observations which support the view that the cyanosis in bronchopneumonia of influenza is due to (1) much of the blood circulating round nonfunctioning alveoli; (2) uneven ventilation of the functioning alveoli, brought about by increase of dead space. Fatal results are liable to occur suddenly with an already diseased heart when there is congestion in the pulmonary circulation, accompanied, as it must be, by lack of oxygen supply to its tissues.

British J. Dermatology and Syphilis, London

44: 1-56 (Jan.) 1932

Mutual Relation Between Zoster and Varicella. E. Bruusgaard.—p. 1.
*Hitherto Undescribed Disease of Skin. A. Whitfield.—p. 24.
Sclerodermia and Thyroid Tumor. H. Haldin-Davis.—p. 29.

Hitherto Undescribed Disease of Skin.—Whitfield describes an uncommon eruption affecting both sexes in adult life. The eruption is not easy to describe in terms that would distinguish it from other rather indefinite eruptions, most of which are generally grouped under the unsatisfactory name of "parapsoriasis." The following are the chief points: 1. It is generally slightly or markedly irritable. 2. The borders of the patches show almost discrete flat red macules without noticeable alteration of the consistency of the skin. 3. Most important is the well defined telangiectasis visible with the simple lens. The eruption is associated with great predominance in the stool of varieties of streptococcus, sometimes with complete absence of Bacillus coli. This bacteriologic peculiarity of the feces can be foretold by careful examination of the eruption. The name suggested for the disease is "dermatitis colonica."

British Journal of Tuberculosis, London

26: 1-56 (Jan.) 1932

Practice and Principle in Treatment of Tuberculosis. A. Trimble.—p. 15.
Osler and Tuberculosis. W. Stobie.—p. 23.
Modern Conception of Artificial Pneumothorax in Treatment of Pulmonary Tuberculosis. L. S. T. Burrell.—p. 28.

British Journal of Urology, London

3: 353-510 (Dec.) 1931

Transplantation of Ureters into Large Intestine: Submucous Implantation Method: Personal Studies and Experiences. R. C. Coffey.—p. 353.

British Medical Journal, London

1: 45-84 (Jan. 9) 1932

Present and Future of Science and Art of Obstetrics and Gynecology. W. Blair-Bell.—p. 45.
Accidents of Male Climacteric. K. Walker.—p. 50.
*Otitic Hydrocephalus: Report of Three Cases. C. P. Symonds.—p. 53.
*Treatment of Adolescent Coxa Vara. G. Perkins.—p. 55.
Case of Brachial Embolectomy. A. G. Banks.—p. 56.
Etiologic Factors in Hyperpiesia. C. W. C. Bain.—p. 57.
Treatment of Hyperpiesia. W. Edgecombe.—p. 58.

Otitic Hydrocephalus.—According to Symonds, the main points of clinical importance in otitic hydrocephalus are as follows: 1. The most striking feature is swelling of the optic disks. This, with hemorrhage and exudate, frequently amounts to several diopters. In cerebral or cerebellar abscess, on the other hand, the optic disks commonly show no more than a slight venous engorgement. Such a degree of swelling as is encountered in otitic hydrocephalus is rarely seen in a case of abscess and is then usually accompanied by extreme drowsiness and malaise. 2. In striking contrast to the appearance of the fundi in otitic hydrocephalus is the general condition of the patient. Between the attacks of headache and vomiting he is likely to be alert, lively, and of good appetite. The patient with an abscess, on the other hand, generally looks and feels ill, is dull, constipated and without appetite. This point of distinction may be blurred or lost when some other condition, such as a lateral sinus thrombosis, is associated with otitic hydrocephalus. 3. The common situations for abscesses are temporal and cerebellar. By the time symptoms of increased intracranial pressure are evident, a cerebellar abscess will have given rise to definite "localizing signs," of which the most important are nystagmus toward the site of the abscess, and incoordination in the use of the upper limb on the same side. A left temporal abscess also (in the case of a right-handed person) will almost certainly have produced localizing signs in the form of "word forgetfulness." Weakness of the opposite face and a homonymous defect in the opposite visual field are also signs of localizing value in temporal lobe abscess. A right temporal abscess, however, is relatively silent, and the differential diagnosis from otitis hydrocephalus is more difficult. If on the basis of these clinical points of distinction the condition of hydrocephalus is suspected, lumbar puncture should be done, a manometer such as Greenfield's being employed. The characteristic features in hydrocephalus are a high pressure and a normal fluid—that is, no excess of cells or protein. Fluid from a case of cerebral abscess is also likely to show a high pressure, but this is not so high as in hydrocephalus. Taking the average normal pressure as 150 mm. of water, the pressure in abscess may be from normal up to 250, while in hydrocephalus it is more commonly in the neighborhood of 300. Finally, the fluid in a case of cerebral abscess is never normal. Usually there is a small excess of cells (mainly lymphocytes with a few polymorphs); always there is an excess of protein. The diagnosis being settled by these means, the condition of otitic hydrocephalus will clear up if treated by lumbar puncture. Enough fluid should be removed on each occasion to bring the pressure to normal, and the procedure should be repeated so long as evidence (symptomatic or manometric) of increased pressure persists. Any local condition such as mastoiditis or lateral sinus infection should be treated on its own merits, but the existence of hydrocephalus is not in itself an indication for operative intervention.

Treatment of Adolescent Coxa Vara.—Treatment for a slipping of the upper epiphysis of the femur is summed up by Perkins as follows: 1. When the slipping is gradual and incomplete, relief of weight bearing must be maintained until the new position has been consolidated. 2. When the slipping is rapid and complete, gradual correction should be done by skeletal traction, followed by relief of weight bearing until the new position is consolidated. 3. When the sequel to the consolidation in the new position is an alteration in the arc of movement at the hip, leading to loss of function, a subtrochanteric osteotomy is necessary. 4. When the sequel is a persistent arthritis of the hip, the hip joint should be arthrodesed.

Journal Obst. and Gynec. of Brit. Empire, Manchester

38: 743-966 (Winter) 1931

Physiology of Menstruation: Its Relation to Etiology and Treatment of Functional Uterine Bleedings. D. J. Cannon.—p. 743.
*Bacteriuria in Pregnancy, Labor and Puerperium. Gladys H. Dodds.—p. 773.
Relation of Vaginal Reaction and Flora During Pregnancy to Occurrence of Puerperal Sepsis. W. R. Logan.—p. 788.
Some Observations on Causes of Human Sterility. S. R. Meaker.—p. 807.
Dystocia Due to Dilatation of Urinary Tract in a Fetus. T. N. A. Jeffcoate.—p. 814.
Influence of Age on Labor. W. C. W. Nixon.—p. 821.
Medical Induction of Labor at City of London Maternity Hospital: Three Hundred and Thirty-Eight Cases. R. L. Dodds.—p. 827.
Cervicitis and Its End-Results. R. F. Matters.—p. 833.
*Primary Papillary Carcinoma of Fallopian Tubes. N. Gupta.—p. 839.
Modification of Fothergill Operation for Prolapse. A. Gough.—p. 844.
Hydramnios: Theory and Argument. J. R. Goodall.—p. 847.
Rupture of Uterus After Classic Cesarean Section. R. E. Tottenham.—p. 851.

Bacteriuria in Pregnancy, Labor and Puerperium.—Dodds reports that 87.2 per cent of specimens of urine obtained from 793 antenatal, parturient and puerperal women were sterile; a colon bacilluria was found in 5.7 per cent, and bacteriuria due to organisms other than Bacillus coli in 5.05 per cent. From 406 consecutive antenatal patients, 88.6 per cent of specimens of urine were sterile; a colon bacilluria was found in 7.6 per cent, and bacteriuria due to organisms other than Bacillus coli in 3.6 per cent. From 105 patients in labor, 94.3 per cent of specimens of urine were sterile; a colon bacilluria was present in 4.7 per cent, and bacteriuria due to organisms other than Bacillus coli in 0.95 per cent. From 281 normal puerperal patients, 85.4 per cent of specimens of urine were sterile; a colon bacilluria was found in 4.9 per cent, and bacteriuria due to organisms other than Bacillus coli in 9.6 per cent. Twenty (2.64 per cent) of the 793 antenatal, in labor, and puerperal patients had inflammation of the urinary tract. Seven (11.8 per cent) of the 59 patients with morbid puerperia had inflammation of the urinary tract. The author believes that the presence of a few pus cells, even in the uncentrifugated urine, is of no importance, provided organisms are absent on culture. Pus cells in the uncentrifugated drop of urine are not of importance even though organisms other than Bacillus coli are found on culture. Pus cells and organisms in the uncentrifugated drop of a fresh catheter specimen of urine are diagnostic of inflammation of the urinary tract. If organisms are found on microscopic examination of the uncentrifugated drop, even though pus cells are found only in the centrifugated drop, an inflammation of the urinary tract may ensue. The danger of catheter infection, when the catheterization is carefully performed, is slight. Repeated examinations of patients with colon bacilluria showed, with two exceptions which may have been due to contamination, that the bacilluria was not temporary. The bacilli found at the successive examinations were morphologically indistinguishable. Colon bacilli may be present in the bladder of pregnant women and not give rise to any clinical signs of inflammation. What happens depends on the virulence of the bacillus and the resistance of the patient. Repeated observations of patients with bacteriuria due to organisms other than Bacillus coli showed, with one exception, that this bacteriuria was present on only one occasion. No relation was established between bacteriuria and parity, period of pregnancy, septic foci, toxemia, previous renal disease or morbid puerperium.

Primary Papillary Carcinoma of Uterine Tubes.—According to Gupta, neoplasms of the uterine tube are rare, and of these carcinoma is the most rare. The rarity of neoplasms in the uterine tubes seems to point to a comparative immunity of these structures to autonomous growth, notwithstanding the irritation to which they are so much exposed. The cause, as in cancer in general, is not known, though many advocate inflammation as a causal factor. Salpingitis is common in gynecologic practice, but the rarity of malignant tumors is such that inflammation as the chief etiologic factor is hardly tenable. In a case observed by the author the malignant uterine tube was associated with an ovarian cyst on the same side, the cyst being a simple unilocular one. There are no characteristic physical signs or symptoms; pain is common but not an invariable symptom. The signs and symptoms are similar to those of salpingitis. Diagnosis of simple from malignant papilloma and from adenocarcinoma cannot be made by clinical means, in the absence of evidence of metastases. The gross specimen resembles a chronic salpingitis. The uterine tube appears as a hydrosalpinx, a tuboovarian cyst or a pyosalpinx. When the tube is opened, a papillomatous growth is often noted. There is hardly any difference in gross appearance between a benign papilloma and a papillomatous carcinoma. It is in histologic sections that the true nature of the growth is revealed. The author believes that it is advisable to open uterine tubes, which are removed surgically in the operating room, and to look for any growth in them. In view of its presence, the whole uterus with its adnexa should be removed.

Medical Journal of Australia, Sydney

2: 799-828 (Dec. 26) 1931

Tuberculous Hip. R. B. Wade.—p. 799.
Tuberculous Disease of Hip Joint. D. J. Glissan.—p. 803.
Report on Use of Gas Anesthesia, 1925-1930. G. Kaye.—p. 804.
Extrarenal Factors in Diuresis. C. S. Hicks.—p. 810.
Saturnine Renal Dwarfism. L. J. J. Nye.—p. 813.
An Alleged Action of Orally Administered Insulin. B. Corkill.—p. 816.

Practitioner, London

128: 1-112 (Jan.) 1932

Infectious Diseases in Public Schools, Their Origin, Spread and Prevention. L. R. Lempriere.—p. 1.
*Febrile Attacks. W. Attlee.—p. 13.
*Practical Aspects of Measles. W. Gunn.—p. 19.
Some Aspects of Mumps: Review of Recent Literature. J. D. Rolleston.—p. 31.
The Control of Scarlet Fever. N. Hallows.—p. 40.
*Diphtheria. W. T. Benson.—p. 46.
*Nondiphtheritic Sore Throats. R. S. Stevenson.—p. 57.
Treatment of Whooping Cough. A. J. Turner.—p. 66.
Miners' Nystagmus, Its Symptoms, Etiology and Treatment. F. O'Sullivan.—p. 71.
Erythredema or Pink Disease. G. Willcocks.—p. 87.

Febrile Attacks.—Attlee states that febrile attacks account for a large part of a school physician's work, and a boy or a girl "with a temperature" is one of the commonest cases he is asked to see. The heat-regulating mechanism seems to be easily disturbed during adolescence, and some individuals at that age become feverish on slight provocation. Broadly speaking, it can be said that fever in adolescence takes the place of vomiting and convulsions in infancy. In school practice, febrile attacks can be divided into two groups according as they occur singly or in batches. Those occurring singly are extremely common and hardly a day passes in a large school without one or two inmates being affected in this way. Those occurring in batches do so at irregular intervals and are clearly infectious. Bed should be insisted on in even the mildest febrile attack until the temperature has been normal for twenty-four hours, and for longer if the attack has been at all severe. During epidemics, and if relapses are common, or if the resulting debility is great, a longer period in bed is desirable. At the beginning of an epidemic, and until its vagaries are known, it is wise to err on the safe side. Free ventilation is essential. Some of the patients do better when the initial purge is omitted and a saline or mild laxative is substituted. Plenty of fluid should be given, such as lemonade, orangeade, tea, jellies and abundance of sugar. Milk, cereals and fruit are better omitted for the first twenty-four hours.

Practical Aspects of Measles.—According to Gunn, convalescent serum and whole blood have been employed in the treatment of the acute stage of measles, but the results obtained hitherto have not been encouraging. Probably a more generous dosage, given early, in the catarrhal stage preferably, would mitigate the severity of the attack, but, at present, supplies are too scanty to institute serum treatment on an adequate scale. Even large doses of serum fail to produce any alleviation in the later stages when complications threaten; this failure is probably due to the presence of secondary invaders as the causal agents of complications. The suggestion to use antistreptococcal or antipneumococcal serums for lung complications is rational, provided one could ascertain the nature of the infecting organism during life. No specific remedy for measles is mentioned as none are available. The latest so-called specifics, amidopyrine and ultraviolet ray therapy, have not exerted any beneficial action on the disease, in the author's experience, either in mitigating the attack or in preventing complications. Convalescence is generally rapid, but all patients benefit by a

generous dietary, suitable exercise in the open air, and a cod liver oil and malt preparation, preferably irradiated. With these measures, the development of chronic bronchitis and recurrent pneumonia, or tuberculosis in its various forms, has become comparatively rare, but there is still need for increased facilities for the convalescence and after-care of measles cases, especially when the hygienic and housing conditions are unsatisfactory.

Diphtheria.—Benson is of the opinion that the only effective method of stamping out diphtheria is by actively immunizing susceptible members of the community against the disease. Susceptibles can be readily distinguished from immunes by the intradermal injection of a minute dose of diphtheria toxin—the Schick test. Three intramuscular injections of diphtheria prophylactic (toxoid-antitoxin mixture, toxoid-antitoxin floccules) at intervals of fourteen days will render the majority of susceptible individuals immune to diphtheria within six months. The method is absolutely safe. A child should be immunized early in the second year. The preliminary Schick test may be omitted. In the immediate presence of diphtheria, an effective passive immunity can be attained within a few hours by the subcutaneous injection of 1,000 units of diphtheria antitoxic serum; this immunity can be relied on for at least a fortnight.

Nondiphtheritic Sore Throats.—Stevenson believes that the first and most important point to be noted in discussing nondiphtheritic sore throats is that one must make quite certain that a sore throat is in fact nondiphtheritic and not diphtheritic. The fact that a membrane is present is of itself no criterion of diphtheria; most of the cases the author has seen with extensive membrane all over the fauces proved not to be diphtheria at all. The so-called typical foul odor of a diphtheritic throat is very like the so-called typical fetor of Vincent's angina. The patient with diphtheria usually looks much more ill, considering the comparatively slight lesion in the throat, than a patient with a nondiphtheritic sore throat. Laryngeal diphtheria is usually considered of more serious significance than faucial diphtheria. It must be remembered, too, that a case of undoubted scarlet fever with a membranous throat may include a genuine infection with diphtheria as well as the scarlet fever. In diphtheria the onset is comparatively slow and insidious, and the temperature is usually only about 99 or 100 F.; but much the same conditions obtain in Vincent's angina. In diphtheria the submaxillary glands are enlarged only on the affected side, while in nondiphtheritic sore throats the submaxillary glands are usually enlarged on both sides. In diphtheria, too, at least in the early stages, the knee jerk is usually absent; but the practitioner must never rely on any of these signs and symptoms when making a diagnosis of a nondiphtheritic sore throat. There is only one infallible sign, and that is the presence or absence of the Klebs-Loeffler bacillus on bacteriologic examination of a swab taken from the throat. Until the diagnosis is established in a suggestive case the patient should be treated for diphtheria. There is a rule that every practitioner should lay down for himself: If a throat is suggestive enough to swab, it is suggestive enough for the patient to have antitoxin injected. The antitoxin should be injected (from 8,000 to 10,000 units intramuscularly) without waiting for the result of the examination.

Tubercle, London

13: 145-192 (Jan.) 1932

*Value of Various Methods of Treatment with Regard to Disappearance of Tubercle Bacillus from Sputum. P. V. Benjamin.—p. 145.

Treatment and Tubercle Bacilli in Sputum.—Benjamin presents evidence that sanatorium treatment alone without additional methods can as a rule be considered sufficient for pulmonary tuberculosis in its earlier stages. In fact, the additional methods which are of such value in stage III cases do not appear to be necessary in stage I and II cases, in order to render the patients bacilli free. One can hope to discharge only a small percentage of patients free from tuberculosis in the stage III group by sanatorium treatment alone. In a large number of these cases additional methods of treatment are necessary such as artificial pneumothorax, cauterization of adhesions, thoracoplasty and phrenic evulsion. When these methods are adopted, the disappearance of bacilli is over 100 per cent better than that obtained by sanatorium treatment alone.

Lyon Médical

148: 765-796 (Dec. 27) 1931

Spasmodic Type of Angina Pectoris. A. Dumas.—p. 765.
Chrysotherapy in Syphilitic Tuberculous Persons. M. Cordier.—p. 774.
*Duodenal Intubation in Parasitic Infestations of Intestinal and Biliary Tracts. L. Morénas.—p. 776.
Epinephrine Content of Suprarenals in Hyptertension and in Addison's Disease. L. Langeron and M. Paget.—p. 780.

Duodenal Intubation in Parasitic Infestations of Intestinal and Biliary Tracts.—Morénas asserts that duodenal intubation is of great scientific interest to the parasitologist, since it aids in the verification of the habitat of certain protozoa of the intestine and (after injection of magnesium sulphate) of the gallbladder. For the clinician this method serves as a valuable aid in the diagnosis of parasitic infestations of the intestine (helminthiasis, protozoal enterocolitis, amebiasis) and of the biliary tract (hepatic distomatosis, hydatid cysts, protozoal infestation of the biliary tract). The duodenal contents will demonstrate the vegetative forms of protozoa that are present as cysts in the stools. Helminthiasis may most practically be diagnosed coprologically, but flagellates such as lamblia, chilomastix and trichomonas, especially when the cysts are absent from the feces, are most easily demonstrated in the vegetative form in the duodenal contents. Amebiasis, more particularly in colitis than in enteritis, is best diagnosed coprologically, but the ameba may also be found in the duodenal contents. Duodenal intubation is particularly indicated in infections of the biliary tract. Hepatic distomatosis is difficult to diagnose; there is present a hepatomegaly with intoxication or sometimes merely a syndrome of obstruction of the biliary tract; the ova of the trematodes may be demonstrated in the bile. In hydatid cysts of the biliary tract the echinococcus also is present in the bile. As for chronic angiocholecystitis of protozoal origin, the centrifugated sediment of the bile will often demonstrate the presence of lamblia, chilomastix and sometimes trichomonas and even Endamoeba dysenteriae. From a therapeutic point of view, duodenal intubation is a useful means of control in treatment and is itself a therapeutic adjuvant in the administration of medicaments.

Paris Médical

2: 505-536 (Dec. 19) 1931

Gynecology in 1931. Huard and Rousset.—p. 505.
Anomalies of Contraction of Uterus During First Period of Labor. C. Jeannin.—p. 514.
*Fever of Pregnancy. A. Fruhinsholz.—p. 518.
Operative Indications in Genital Prolapse. A. Schwartz and S. Huard.—p. 520.
Obstetrics in 1931. J. Ravina.—p. 526.
*Partial Conservation of Ovary. E. Villard and J. Caillot.—p. 531.

Fever of Pregnancy.—Fruhinsholz noted that some women, otherwise in good health, during the early period of pregnancy after the disappearance of the menses registered a slight rise in temperature above the normal. This increase was to the extent of several tenths of a degree centigrade. Women normally registering a mean temperature of 37 C. (98.6 F.) during gestation toward evening had rectal temperatures of 37.5, 37.8 or even 38 C. (99.5 to 100.3 F.). Some women were keenly aware of this thermic elevation, others only on examination. This febrile condition, however, did not persist after the first half of the period of gestation. Comparison of thermic curves demonstrated a similarity with normal rise of temperature following disappearance of the menses. The author concludes that a shift in temperature during gestation up to 38 C. (100.3 F.) does not necessarily have pathologic significance. However, changes in temperature should be carefully watched and compared with the mean temperature. A mean temperature of 36 to 36.5 C. (96.8 to 97.7 F.) may increase to 37 or 37.5 C. (98.6 to 99.5 F.). The change in temperature may be a physiologic phenomenon, probably endocrine in origin, since the activity of the corpus luteum is limited to the same period in which hyperthermia prevails.

Partial Conservation of Ovary.—Villard and Caillot assert that in speaking of partial conservation they mean the preservation of the ovary on one side, the other ovary being removed in its entirety, and in every case with the preservation of the uterus. Indications for ovarian resection should depend on clinical manifestations. They have had occasion to observe the results in forty-seven interventions before 1929 and in more

than fifty interventions since that time: these included conservation of the uterus and partial conservation of the ovary. All the forty-seven patients especially considered were young women, the oldest being 40 years of age. The menses returned usually after the first or second month in 98 per cent and became regular and normal in 92 per cent of the patients. In seven patients the menses were irregular or a little painful. There was one failure: conservation for bilateral cystic ovaritis in which the menses did not appear and the patient presented endocrine disturbances. Fertility was preserved in twenty-seven patients, four becoming pregnant and delivery being performed at term. There was no record of fatality. The authors conclude that a minimal preservation of ovarian tissue will assure complete ovarian function: fertility in case of tubal permeability, and menstruation in case of conservation of the uterus. Partial conservation of the ovary with integrity of the tubes is possible in benign bilateral tumors of the ovaries (as dermoid cysts). In bilateral inflammatory lesions of the tubes, ovarian conservation may permit fertility in rare cases of tubal restoration; it will assure menstruation after bilateral salpingectomies with conservation of the uterus and will avoid endocrine disturbances of ovarian origin.

1: 1-32 (Jan. 2) 1932

Tuberculosis in 1932. P. Lereboullet and M. Lelong.—p. 1.
*Substitution Effusions of Artificial Pneumothorax. E. Rist and P. Véran.—p. 12.
Surgical Treatment for Pulmonary Tuberculosis. A. Maurer.—p. 15.
*Bilateral Collapsotherapy in Pulmonary Tuberculosis. M. Léon-Kindberg.—p. 18.
Seasonal Factors in Evolution of External Tuberculosis. M. and G. Mozer.—p. 22.
*Subpleural Removal of Adhesions in Artificial Pneumothorax. D. Douady and A. Meyer.—p. 25.

"Substitution Effusions" of Artificial Pneumothorax.—Rist and Véran assert that an interruption of a pneumothorax by substitution effusions is not uncommon. (Among 226 patients, interruptions occurred in 6 per cent). They review seven typical cases in which they find that the appearance of these accidents is insidious and is characterized clinically by dyspnea with effort or a distinct pleuritic syndrome. The effusions are variable, sometimes abundant, serofibrinous, puriform, hemorrhagic or cholesteric; they are slightly inflammatory and are not accompanied by great inconvenience; they occur in patients with pulmonary tuberculosis, which remains cured from one to ten years after the resorption of the pneumothorax. The tuberculous nature, however, is demonstrated from the tenth to the twelfth day after inoculation of guinea-pigs by the lymph node or subcutaneous routes. The presence of the effusions should be recognized in patients who have had a pneumothorax performed and in whom the pleura has remained dry for several years but who suddenly complain of dyspnea on exertion or present pleuritic signs. Opacity of the pleura in roentgenograms can be easily confused with fibrothorax or dry localized pachypleuritis. Exploratory puncture is a certain method of diagnosis. Regular examination is necessary in patients in whom a development of such effusions is possible. Clear or bloody effusions disappear spontaneously; but, if the effusions are very abundant, evacuation and institution of pneumothorax is indicated and resorption may result without any other accident. Purulent effusions should be carefully watched. A temporary oleothorax may help to prevent another development of exudate.

Bilateral Collapsotherapy in Pulmonary Tuberculosis.—Léon-Kindberg asserts that the existence of bilateral pulmonary lesions had long been an obstacle in treatment. He discusses secondary bilateral pneumothorax, simultaneous bilateral pneumothorax and preventive bilateral pneumothorax in view of his own observations and observations in the literature. Bilateral pneumothorax therapy is recent. His own twenty-six interventions resulted in seven complete recoveries and six still in the course of treatment with uncertain prognosis. He believes that bilateral collapsotherapy should be limited most generally to localized lesions in patients whose general condition and physical capacity are well recognized and included in the indications for treatment. Bilateral pneumothorax gives results that are interesting scientifically; it permits the prolongation of life and cure of a number of patients with a fatal prognosis. Unilateral pneumothorax should, however, be the first measure for treatment and if performed early enough will not necessitate the bilateral intervention that is usually necessary when in a large number of cases diagnosis for treatment has been too long delayed.

Subpleural Removal of Adhesions in Artificial Pneumothorax.—Douady and Meyer discuss the Jacobaeus operation with the modifications of Maurer and compare it with other methods recommended for the removal of pulmonary adhesions. The newer method does not consist in intrapleural section but in a subpleural disinsertion or detachment at the base of the adhesion. The adhesions may be of four kinds. One, which consists of a band in the form of a thread or thin velum, is the same width at the point of pulmonary insertion as at the parietal implantation; the second type of adhesion is wider at the thoracic insertion; the third appears in the form of a cone with the lung as the base, and the fourth consists of a wide band, the pulmonary insertion and the parietal insertion both widened. The intervention is such as to bring about disinsertion in a zone absolutely free of pulmonary tissue and the tissue is cut by a process that prevents hemorrhage when one is forced to work in the thoracic wall in contact with the intercostal vessels. Maurer has contrived a combined cautery which consists of a platinum loop mounted on a special body which can furnish either an electric current in the form of a red hot flame or a high frequency coagulation current. The two phenomena of coagulation and section are included in one instrument. A system of pedals permits the operator to follow the one by the other. This has some advantage over the electric bistoury. The amperage helps to designate at each instant the nature of the tissue in contact with the point of the instrument. The electric cautery produces a zone of coagulation 2 mm. wide in dry tissue, without burning and without loss of blood. Previous to operation, anesthesia is obtained by the injection of several cubic centimeters of a 1:400 solution of procaine hydrochloride. The endopleural route is used and the long needle is guided by the pleuroscope. The actual time of operation varies according to the width of the adhesion, sometimes several minutes and then again one or two hours; sometimes it is more satisfactory to perform a partial operation to be completed after an interval of several weeks. The author recommends this intervention if the pleura is normal in aspect but recommends caution when the pleura is diseased, the effusion is cloudy and tubercles are numerous on the thoracic wall, on the lung and on the adhesions.

Presse Médicale, Paris

39: 1917-1932 (Dec. 30) 1931

Clinical and Pathogenic Study of Accidents of Sensitization to Insulin. A. Cade, P. Barral and J. Roux.—p. 1917.
Hepatic Form of Infantile Kala-Azar. R. Poinso.—p. 1920.
Study of Biologic Properties of Tuberculous Exudates and Tubercle Bacilli: Their Value in Order to Understand Immunity in Tuberculosis. Y. Nedelkovitch.—p. 1922.
*Further Observations on Intravenous Injections of Alcohol. M. Fejgin.—p. 1925.

Further Observations on Intravenous Injections of Alcohol.—Fejgin states that he has obtained undoubted favorable effects from intravenous injections of alcohol in nonspecific purulent complications of pulmonary disorders. Thirty-three per cent alcohol is used in daily injections of 15 to 20 cc., continued as long as the condition of the patient demands it and depending on the local reaction of the veins; this may at times force suspension of the injection for several days. Results obtained consist in slowing up of the pulse, increasing strength of the patient, diminishing cough and expectoration, lowering of the temperature and general feeling of well being, while no detrimental effects attributable to alcohol have been noted.

40: 17-40 (Jan. 6) 1932

*Orthostatic Hypotension. C. Laubry and E. Doumer.—p. 17.
Epileptogenous Vegetative Center in Diencephalon. A. Salmon.—p. 20.

Orthostatic Hypotension.—Laubry and Doumer give this name to a syndrome characterized by an important fall in the arterial pressure of the patient on changing from the dorsal decubitus to the erect position and resulting in typical disturbances. Five case histories are offered to prove the extreme similarity of the symptoms. The fall in arterial pressure is never less than 4 cm., may reach 8 cm., and is persistent, lasting for days, weeks and even months. Resulting functional disturbances vary in intensity, duration and evolution. Lipo-

thymia is a common symptom; the patient accuses dizziness and fainting spells, which are due to beclouded mental state and weakening of vision resulting from habitual cerebral ischemia; he suffers from abortive syncopes, more or less recurrent. The trouble must be imputed to a defect in the regulatory mechanism of the blood pressure. This mechanism in hypertension as well as in hypotension keeps the pressure constant around its acquired tensional level, while in orthostatic hypotension the mechanism seems to have become indifferent to the changes in pressure resulting from changes of bodily position. The authors admit that nothing definite is known about the causation of this failure of the mechanism and expound the currently held theories. The syndrome is differentiated from idiopathic permanent arterial hypotension, recently described, by its important fall of pressure accompanied by subjective disturbances depending undoubtedly on it. Arterial hypotension gives only the illusion of a hypotension which does not exist in reality and indicates purely a degree of circulatory aplasia. Its remaining symptoms are not pathognomonic and are encountered just as well in hypertension; they are syncope, acrocyanosis and asthenia; even the figures given in support of its existence are open to discussion and the condition is frequently encountered in perfectly normal young subjects. Prognosis of orthostatic hypotension is favorable. Treatment consists in rest, psychotherapy and physical therapy; epinephrine may be used but is not to be relied on.

Semaine des Hôpitaux de Paris

7: 627-658 (Dec. 31) 1931

*Clinical and Functional Study of Mongolism. R. Turpin.—p. 630.
Pernicious Anemia. E. Pichon.—p. 641.
Frequency of Sporadic Cases of Heine-Médin's Disease. J. Chauveau.—p. 649.
Tuberculous Meningitis Simulating a Parkinsonian Syndrome: Case. J. Lévy-Valensi and Mme. Markarian.—p. 653.

Mongolism.—Turpin uses the term "mongolism" to cover pseudomongolian dystrophy with mental retardation. During the last two years the author has had a chance to study twenty-seven patients. He took occasion to study the physiognomy, the osteomuscular system, lingual and dental anomalies, digestive and respiratory functions, congenital dystrophies and malformations, endocrine and metabolic disturbances, and mental retardation with neuropsychic peculiarities. Roentgenography demonstrated a global retardation, less regular than in myxedema, and disturbed exceptionally by a discordant prematurity. Muscular hypotonia with ligamentary laxity was a common symptom; congenital cardiopathies were frequent; other congenital malformations were syndactylia of the fingers and toes, polydactylia, micromelia, anal imperforation, supernumerary pulmonary lobes, hermaphrodism, spina bifida and harelip. The results obtained from the study of the endocrine system were inconstant. The pseudomongolian dystrophy could not be attributed to any particular glandular disturbance. A retardation in sexual development accompanied the general disturbances. Feeblemindedness associated with the special physiognomy was a second characteristic element of mongolism. This included neuropsychic peculiarities, motor and sensory disturbances, general psychic deficiencies (emotion, imitation, memory, attention). Among all the psychic or mental peculiarities, however, the author could not designate a single sign that could be termed pathognomonic for mongolism.

Diagnostica e Technica di Laboratorio, Naples

2: 925-1012 (Nov. 25) 1931

*New Method for Qualitative and Quantitative Estimation of Bilirubin in Urine with Daddi's Diazo Reaction. A. Greco.—p. 925.
*Technic for Estimation of Amino Nitrogen in Blood with van Slyke's Gasometric Method. G. Sannicandro.—p. 933.
Quantitative Determination of Red Blood Corpuscles in Hematuric Urine. F. Volante.—p. 944.
Value of the Hench-Aldrich Reaction for Determination of Urea in the Blood. E. Pedone.—p. 953.

Estimation of Bilirubin in Urine.—Greco describes the different steps taken to improve on and to adapt Daddi's diazo reaction to the estimation of bilirubin in urine, and prescribes the following definite procedure: To 7 cc. of absolutely fresh, acid urine, 3 cc. of a 10 per cent solution of barium chloride is added. The mixture is centrifugated and the precipitate is washed several times. To the precipitate, 2 cc. of a decinormal alcoholic solution of potassium hydroxide is added. The mixture is shaken for one minute and centrifugated again. The alcohol is decanted into another test tube. Six drops of freshly prepared Daddi's reagent (potassium isoparanitrodiazobenzol) in a 5 per thousand aqueous solution is added and then 0.5 cc. of concentrated sulphuric acid. The presence of bilirubin (even of 1 part in 1,000,000) will produce a sudden reddish purple coloration turning definitely purple in a few seconds and becoming more intense within the next fifteen to twenty minutes. After this lapse of time the bilirubin content, expressed in milligrams per cubic centimeter, is read from a special diagram used with the colorimeter of Autenrieth.

Estimation of Amino Nitrogen in Blood.—Sannicandro finds fault with van Slyke's method because the urea remaining in the filtrate after treatment of the blood serum with 20 per cent trichloracetic acid gives rise to errors in overestimation of amino nitrogen running as high as 50 per cent. Experiments made by the author prove that amino-acids have great affinity for nitrous acid and that urea in the same reaction loses part of its nitrogen. In order to eliminate this undesirable result he uses an 8 per cent solution of mercury nitrate with addition of exactly 6.5 cc. of dilute (1:10) nitric acid to precipitate the urea. This solution does not precipitate amino-acids whether unmixed or mixed with urea. The author explains the steps of the various experiments that prove his statements and concludes that, although van Slyke's gasometric method of estimating amino-acids in ordinary solutions remains unquestioned, it is erroneous in the added presence of urea such as obtains in the blood serum and can be used only after removal of the urea from the serum.

Policlinico, Rome

39: 45-84 (Jan. 11) 1932. Practical Section

*Variations of Ketonemia in Liver Disorders. C. Toscano.—p. 45.
*Fracture of Base of Cranium: Case. G. Muzzarelli.—p. 49.

Variations of Ketonemia in Liver Disorders.—Toscano, on studying the changes in ketonemia in twenty-eight cases, reached the conclusion that an increase in the ketone bodies of the blood points to a diffuse lesion of the hepatic parenchyma. He found also that a functional change in the liver may cause a disturbance in the ketone exchange and a consequent increase in the ketone bodies of the blood.

Fracture of Base of Cranium.—Muzzarelli describes a case of fracture of the left half of the cranium, which spread and affected the whole base of the cranium. He explains the mechanism of the action of traumas of the cranium in general. He considered, on the basis of the symptoms presented, that in his case the condition was doubtless due to the path followed by the line of fracture. He gives the reasons for the survival of the patient in spite of the exceptional gravity of the trauma, and calls attention to the interest of the case, owing to the combination of rather simple syndromes into a highly complex and rare syndrome.

Rassegna di Clin., Terap. e Scienze Affini, Rome

30: 303-352 (Nov.-Dec.) 1931

Presence of Myelinated Fibers in Hypophysis of Man. E. Trocello.—p. 303.
Behavior of Reticulo-Endothelial System in Experimental Hemolytic Anemias of Healthy and Splenectomized Animals. M. Bormioli.—p. 306.
Hormones and Muscular Work. G. del Guerra.—p. 322.
Syndrome of Acute Intestinal Obstruction of Enlarged Colon in Renal Colic. P. Piazza Sormani.—p. 329.
Hemostasis with Calcium Therapy in Hemoptysis. A. Benincori.—p. 336.
*Treatment of Typhoid with Extract of Thymus. B. Boggian.—p. 339.

Treatment of Typhoid with Extract of Thymus.—Dissatisfied with the results obtained in typhoid by the recognized modes of treatment, Boggian has used lately in eleven cases of typhoid and four cases of paratyphoid a preparation of 2.5 per cent sodium thymonucleinate. The daily doses used have varied from 2 to 10 cc. of the preparation according to the age of the patient and were regulated with the view of obtaining the highest rate of reactionary leukocytosis, the maximum dose being seldom needed. The most favorable results have occurred from the administration of average doses and consisted in a rapid decrease of the temperature stabilized in the lower ranges after two or three injections, an improvement in the general condition and the heart action and a notable shortening of the course of the disease. Especially in three serious cases with delirium, small, very rapid and irregular pulse, the clinical

symptoms improved so suddenly as to exclude any possibility of coincidence. The author recommends further trial of thymus extracts in typhoid.

Archivos Españoles de Pediatría, Madrid

15: 705-768 (Dec.) 1931

*Treatment of Cholera Infantum. S. E. Burghi.—p. 705.
Provoked Extravasation to Determine Resistance of Skin Capillaries. E. Jaso.—p. 720.
Vomiting in Infants: Intolerance to Mother's Milk. M. Macein.—p. 729.

Treatment of Cholera Infantum.—Burghi discusses the treatment of cholera infantum from three points of view: prophylaxis, treatment of the disease, and realimentation of the patients. Prophylaxis includes protection of infants against dystrophy, infections, dehydration and excessively high temperatures. Infants should receive the proper qualitative and quantitative diet. They should be fed preferably with human milk and if there is not a sufficient amount of it the diet may be supplemented with other milk. They should be given a sufficient amount of water to keep the water balance in proper condition. In warm days, infants should be kept in cool places and should wear light clothes. Any infection (even if it appears benign) should be treated. The two principal aims of the treatment should be to check the acidosis and to restore the water balance by rehydrating the patient. Acidosis and dehydration are two interrelated conditions. In order to compensate the intense loss of water from the tissues and also to restore the water content of the blood, the patient should be given every day from 1,200 to 1,500 cc. of water by mouth and also large amounts of fluids, by the subcutaneous, intraperitoneal or intravenous route. The author uses with satisfactory results either one or two daily subcutaneous injections of 75 or 100 cc. of a hypertonic 10 per cent solution of dextrose diluted with one third its volume of Ringer's solution, or intraperitoneal clysters of from 200 to 400 cc. of a weak solution of sodium chloride. (The author does not specify the concentration of the solution.) Dextrose solutions when given either subcutaneously or intravenously have both a therapeutic and a nutritional effect. The patient is also given one or two daily injections of 0.5 cc. each of a 5 per cent solution of camphor in oil. The injection should be made slowly, because camphor when injected may cause convulsions. If the patient shows a tendency to collapse, he should be given a bath at 38 C. for five or ten minutes, two or three times a day. A transfusion every day, for three or four days, with 60 or 80 cc. of the mother's blood is indicated in athreptic infants with grave forms of the disease. While symptoms of alimentary toxemia persist and the type of the diarrhea is not modified, that is, during twenty-four or thirty-six hours, the patient should be given only a water diet. From that time on, he should be given either a diet with human milk (whole or deprived of fat substances) and a complemental water diet with a 10 per cent content of albumin milk, or albumin milk with a small percentage of sugar. In both cases the alimentary substances are slowly increased as soon as the patient's condition and the type of the diarrhea improve, first to a maintenance diet (70 calories per kilogram of body weight) and later on to a complete diet (100 calories per kilogram of body weight) to fulfil the requirements of the patient. Both during the acute period of the disease and during the convalescence, the patient should receive liberal amounts of water.

Brasil-Medico, Rio de Janeiro

45: 1205-1228 (Dec. 26) 1931. Partial Index

*Polymorphism of Tubercle Bacillus. A. Fontes.—p. 1205.

Polymorphism of Tubercle Bacillus.—Fontes believes that there are several types of mutation of tubercle bacilli: the degeneration of virulent into nonvirulent forms, sometimes into entirely harmless bacteria (a mutation which may be caused by lytic changes of genuine tubercle bacilli), the development of genuine tubercle bacilli from forms of a lower virulence, and a characteristic mutation of certain pathogenic types of tubercle bacilli to paratuberculous acid-resistant forms and later to nonacid-resistant and diphtheroid forms of an attenuated virulence. His theory is supported both by the observation of the evolutive cycle of tubercle bacilli after the inoculation of infected material into guinea-pigs and by the cultivation in vitro of tubercle bacilli from tubercle ultravirus. The tubercle bacillus passes through a definite developmental cycle. Besides the ultravisible forms there are unstainable and therefore also non-acid-fast forms which may be transformed into acid-fast forms and into true tubercle bacilli. The problem of mutation of bacteria is related to several biochemical and pathogenic phenomena, which in the case of tubercle bacilli may be explained by a property of the ultravirus forms to retain primordial inherited characteristics by which the ultravirus may go through several changes with a tendency to develop either an increased virulence or, on the contrary, an attenuation or even disappearance of the virulence. The author states that both in vivo and in vitro it is possible to obtain certain forms of bacteria that cannot be confused with bacteria of contamination and whose development demands special conditions of the medium and of the technic. The author inoculated guinea-pigs with filtrates of cultures of human tubercle bacilli from a case of fatal tuberculous bacillemia and a case each of acute renal tuberculosis and acute pulmonary tuberculosis. Blood cultures prepared in common peptone medium remained sterile for twenty days when colonies of a tetragenic nonresistant diplococcus appeared. The passage of the cultures to new culture tubes with the addition of blood of rabbit and of guinea-pig, respectively, to different tubes, promoted the development of acid-resistant bacteria with the same morphologic and cultural characteristics as those of tubercle bacilli with the only exception that when inoculated into guinea-pigs they were nonvirulent.

Deutsche medizinische Wochenschrift, Leipzig

58: 41-80 (Jan. 8) 1932

Protection of Skin Against Light. H. Meyer and H. Kirchhoff.—p. 41.
Intestinal Malformations: Ileum Duplex or Intramesenteric Meckel's Diverticulum. R. Borrmann.—p. 43.
*Spontaneous Diffuse Subarachnoidal Hemorrhage (Leptomeningeal Spontaneous Hemorrhage). O. Hess.—p. 45.
Primary Oliguria Following Accident: Traumatic Neurosis. G. Strube.—p. 46.
*Treatment of Sepsis, Meningitis and Empyema by Means of Artificial Abscess. L. Jacob.—p. 48.
*Continuous Intravenous Infusion of Dextrose in Treatment of Severe Puerperal Infection. Kirstein.—p. 51.
Milk-Free Diet for Children with Edema. R. Hess.—p. 52.
General Lymphatic Stasis. H. Gross.—p. 53.

Spontaneous Diffuse Subarachnoidal Hemorrhage.—Hess is convinced that diffuse subarachnoidal hemorrhage may occur spontaneously in healthy, especially in young, persons with an intact vascular system. In numerous cases a vasoneurotic diathesis is the cause of the hemorrhagic tendency of the meningeal vessels. However, organic changes of the vascular system, especially a basal aneurysm, should be searched for in every case.

Treatment of Sepsis, Meningitis and Empyema by Means of Artificial Abscess.—Jacob considers it wrong to abandon entirely the old method of the artificial abscess formation by means of subcutaneous injection of oil of turpentine. He admits that in cases of septic endocarditis, in fulminant forms of staphylococcic and streptococcic sepsis, and in puerperal infections with rapid metastasis the artificial abscess is generally ineffective. However, in those cases in which the organism's resistance is sufficient to withstand the first attack of the infection, and there is a prolonged combat between the infection and the organism, the artificial abscess is helpful. Observations in twenty-nine mostly severe cases of sepsis, of suppurative meningitis, or of empyema convinced him that the local inflammation and suppuration produced by the subcutaneous injection of sterile oil of turpentine increases the resistance power of the organism by mobilizing all reserves and thus effects cure. The author shows what he considers the best time for injection of turpentine and emphasizes the leukocyte curve as an indicator of the resistance power. He further discusses the technic and the dosage of the turpentine injection and also the management of the resulting abscess. Of the symptoms that follow the injection he mentions the leukocytosis and the fever. He explains the action mechanism of the artificial abscess as a nonspecific irritation therapy.

Continuous Intravenous Infusion of Dextrose in Severe Puerperal Infection.—Kirstein states that the continuous infusion of a 10 per cent solution of dextrose should be employed in every case of severe puerperal infection. He cites his own observations and those of other authorities, some of whom employed weaker solutions, but he himself still uses the

10 per cent solution. He does not agree with the statement that the continuous infusion is possible only in a hospital and under constant supervision, for he employed it successfully in private homes. He obtained favorable results with continuous intravenous infusion, even in cases that were refractory to other treatments and in patients in whom the attacks of chills persisted after several administrations of streptococcic serum. However, he does not consider the continuous infusion as alone sufficient but employs it in combination with intravenous and intramuscular injection of an iodine preparation and with administration of alcohol. If chills recur as late as two days after continuous infusion has begun, ligation of veins should be resorted to. The author further states that continuous infusion has proved helpful also in peritonitis, and because of its favorable influence on the heart he recommends it for postoperative treatment.

Deutsche Zeitschrift für Chirurgie, Berlin

233: 657-771 (Dec. 30) 1931

Experiments on Operative Shock. F. Metzler.—p. 657.
*Origin and Prevention of "Indirect" Sequelae of Surgical Operations. W. Capelle.—p. 674.
Surgical Diseases of Thoracic Organs Following Operative Intervention on Oral Cavity. R. Nissen.—p. 708.
Patella Partita. W. Siemens.—p. 727.
*Simultaneous Bilateral Rupture of Ligamentum Patellae and Development of Indirect Ruptures of Extension Apparatus of Knee in General. O. Kapel.—p. 756.

Origin of "Indirect" Sequelae of Surgical Operations.—Capelle shows that postoperative pneumonia, thromboembolism and intestinal atony are complex processes. The clinical observation that all three occur most frequently after abdominal interventions indicates the existence of a constant etiologic factor. This factor is mainly of the functional mechanical type and is due to the impairment of the action of the surgically injured abdominal wall. For the latter is a portion of a functional unity of muscles on which depends the "lower" respiration, the optimal circulatory conditions of the vena cava inferior and probably also the energy for the movements of the lower portions of the gastro-intestinal tract. The surgical wound destroys the muscular unity. Since such a disturbance is primarily due to inhibition caused by pain, the main factor in the prophylaxis of the three indirect sequelae of laparotomy is the permanent exclusion of the postoperative pain. The author describes a method of prolonged local anesthesia which he considers suitable for this purpose.

Simultaneous Bilateral Rupture of Ligamentum Patellae.—Kapel maintains that the indirect ruptures of the extension apparatus of the knee occur most frequently during rapid, jerk-like contractions of the quadriceps, while the knee is stretched or half bent, when the person wishes to avert a fall or during jumping. The development of the ruptures is explained by the anatomic attachment of the quadriceps muscle. The condition is similar to that in cases of rupture of the achilles tendon. The author reviews several cases from the literature and describes one of his own observation. As treatment he recommends suture and prolonged immobilization.

Münchener medizinische Wochenschrift, Munich

79: 49-88 (Jan. 8) 1932

New Bandage for Chronic Deforming Inflammation of Hip Joint. Hohmann.—p. 49.
Method for Testing Antirachitic Action of So-Called Nutritional Preparations. L. Wamoscher and A. Schmieden.—p. 51.
*Appendicitis Simulating Gastric Disorder. H. A. Stappert.—p. 54.
Cure in Retention of Urine by Spontaneous Formation of Urinary Fistulas. F. Ronnefeldt.—p. 56.
Recognition and Treatment of Arsenic Poisoning. E. Leschke.—p. 57.
Properties and Therapeutic Action of Mud Baths. S. W. Souci.—p. 62.
New Surgical Probe. P. Fuhrmann.—p. 66.
*Treatment of Pemphigus Neonatorum Gravis. H. Schricker.—p. 67.
*Treatment of Encephalitic Processes with Alcoholic Solution of Turpentine Oil. L. Veilchenblau.—p. 67.

Appendicitis Simulating Gastric Disorder.—Stappert thinks that in many patients who complain about gastric pains the cause is a chronic appendicitis. Careful observation of all patients who came to him with gastric complaints (177 cases) proved to him that in forty-six (26 per cent) appendicitis was certain, and in an additional forty-one cases it was probable.

Treatment of Pemphigus Neonatorum Gravis.—Schricker reports two cases of pemphigus neonatorum gravis. In the first infant local therapy was resorted to but was without effect and the child died. In the second case, cure followed the intramuscular injection of a vaccine preparation. Accordingly the author recommends the latter procedure to prevent the septic complications of pemphigus neonatorum gravis.

Treatment of Encephalitic Processes with Alcoholic Solution of Turpentine Oil.—Veilchenblau found that a 10 per cent solution of turpentine oil in alcohol is much more effective for intramuscular injections in encephalitis than turpentine oil. He illustrates this in four case reports; namely, two cases of epidemic encephalitis, one case of tuberculous meningitis, and one case of postvaccinal encephalitis.

Polska Gazeta Lekarska, Lwów

11: 1-20 (Jan. 3) 1932

Pathogenesis and Immunity in Infections of Air Passages (Influenza, Pneumonia). K. Lewkowicz.—p. 1.
*Clinical and Experimental Value of Fractional Analysis of Stomach Contents. A. Uryson.—p. 4.
Influence of Morsztym Mineral Water on Hydrochloric Acid Secretion of Stomach. J. Eichel.—p. 8.
Surgical Removal of Ovarian Tumors During Pregnancy. T. Zawodziński.—p. 10.
Hypertrophy of Male Breast. R. Hinze.—p. 11.

Clinical and Experimental Value of Fractional Analysis of Stomach Contents.—Uryson drew a number of stomach content secretion curves in his experiments on the activity of the gastric glands and muscles, using the method of fractional analysis. His objects are to find the sum total of secretory activity, the relation of free and combined acid and motility, and the action of some pharmacologic agents. The work is based on 150 hospital cases. The stomach was emptied in the morning by means of a duodenal tube; the patient was fed 30 cc. of 5 per cent alcohol stained with methylthionine chloride; every ten minutes, 20 cc. of gastric contents was withdrawn by aid of the tube until all the color had disappeared. The contents were tested for total acidity, free acid and combined acid. The character of the meal—diluted alcohol, caffeine, sweetened tea or vegetable extracts—did not show any difference as far as the acidity was concerned. Incidentally, no untoward effects of alcohol were noted in these experiments, and the value of the Boas-Ewald method was upset when frequently the first analysis showed hypoacidity and subsequent samples proved beyond doubt the presence of hyperacidity. In a series of seventy-two cases divided between duodenal ulcers, ulcers of the fundus, ulcers of the pyloric end, achylia, gastric atony and simple hyperacidity, the duodenal ulcers produced a "step ladder" character of curve (sudden rise and fall) repeated several times (slight increase and curve variation of total and free acid), with color disappearance in from fifty to sixty minutes. In four cases there was early and marked acidity with speedy emptying (forty minutes); a roentgenogram disclosed increased motility and cicatrization of the pyloric end. In ulcers of the fundus, the curves were atypical and of all types. In ulcerations of the pyloric end (12 cases) the curve has two rapidly succeeding up and down strokes and rapid evacuation (these cases showed more marked increase in acidity than duodenal ulcers). In achylia the curves are flat and the acidity is very low; similar observations were made in cancer of the fundus, in which constant hypo-acidity was noted. A flat curve with acidity below 8 is pathognomonic of pyloric cancer. Similar tests were conducted in thirty-three cases of pulmonary tuberculosis to throw light on the character of acidity curves in this disease and the behavior of acidity in always existing progressive loss of appetite. The results proved absence of relation between loss of appetite and acid secretion. The drugs injected subcutaneously or intravenously during ingestion of the test meal were atropine, histamine, pilocarpine, calcium chloride and insulin. The total number of cases was forty-five. After 0.5 mg. of atropine there was a decrease of free acid but the combined acid remained unchanged; after 1 mg. there was a marked decrease of both. Pilocarpine increases the flow of gastric juice, slightly reduces the total acidity, and produces no variations in the relation between the free and the combined acid. Histamine in small doses (0.025 mg.) increases the total acidity and the free acid; doses over 0.5 mg. produce salivation, anxiety and epigastric pains. Calcium chloride was fed by mouth (1 Gm. three times a day in water) for a week;

then it was stopped and fractional analysis was done. This mode of administration reduced the acidity, while intramuscular and intravenous administration produces no effect on the acidity. Insulin gives a marked increase of total acidity (40 per cent) and the increase in free acid is relatively higher than the increase in the total acid. There was no relation noticed between the blood sugar level and gastric acidity; in insulin hypoglycemia the increase of total acidity was uniformly 40 per cent.

Clujul Medical, Cluj

12: 619-686 (Dec. 1) 1931

*Probability of Internal Secretion of Lacrimal Glands. D. Michail and P. Vancea.—p. 619.
Anatomoclinical Considerations on Epulis. L. Ghidrai and A. Vitalyos. —p. 634.
Relation Between Psychology, Neurology and Psychiatry. G. Preda. —p. 640.
Study of 1931 (February-March) Influenza Epidemic. M. Sireteanu. —p. 650.
Intoxication of Nursling by Poppy-Seeds. I. Iana.—p. 654.

Internal Secretion of Lacrimal Glands.—From numerous researches on the chemistry and pharmacodynamics of extracts of the lacrimal glands, Michail and Vancea conclude that the extracts possess interesting properties distinct from those of all other known organic extracts. Their principal properties include powerful vasoconstriction, cardiotonic action of lacrimal extract A, stimulating action on the uterine muscles, on respiration and on urinary secretion, and reduction of the metabolism of sugars and fats. With reference to the influence of the extracts on oxidation of tissues, they must be divided in two groups: extracts A, which accelerate and extracts B, which inhibit oxidation. Action of the extracts on the blood system consists in polyglobulism with leukocytosis, reduced resistance of the blood cells, and reduction of the metabolism of calcium and phosphorus with concomitant reduction of the hydrogen ion concentration and diminished metabolism of water in the tissues. The extracts also accelerate cicatrization of wounds and stimulate growth. All these pharmacodynamic properties suggest the probability of the existence of an internal secretion in the lacrimal glands and the authors intend to elucidate this in the course of complementary experimentations already initiated. These experiments will establish what general disturbances of the organism follow bilateral and complete extirpation of the lacrimal glands and their pathologic disorders.

Klinicheskaya Meditsina, Moscow

9: 859-937 (Oct.) 1931

*Chronic Keratoconjunctivitis, Pharyngitis and Arthritis with Respect to Endocrine (Especially Ovarian) Deficiency. S. A. Spector. —p. 876.
Symptomatology, Pathogenesis and Clinical Aspect of Hypophyseal Cachexia. V. V. Gerbst.—p. 883.
*Thyroid in Relation to Serum-Atropine Reaction and Serolipoid Content. A. D. Osnovina-Lomovitskaya.—p. 887.
*Treatment of Hypohormonal Amenorrhea by Means of Physical Therapy and an Extract of Urine from Gravida. N. S. Jelokhovtsev. —p. 892.
Roentgen Therapy in Lymphogranulomatosis. M. I. Karlin.—p. 898.
Galvanotherapy in Gastric Disturbances. A. A. Kirstner.—p. 904.
Calcium Iontophoresis in Treatment of Colitis. M. A. Shcheglova. —p. 909.

Chronic Pharyngitis and Arthritis and Endocrine Deficiency.—Spector asserts that certain changes in the conjunctiva, cornea, throat and joints are not due to disturbances in the secretion of specific hormones but are a result of a weakened secretory function in the whole system of endocrine glands. He discusses seven personal observations in which the symptoms were so characteristic that the patients were treated by an ophthalmologist for chronic conjunctivitis, by a laryngologist for chronic pharyngitis, and by an internist for gout or articular rheumatism—and all without result. The analogous symptoms were primarily the absence of lacrimal secretion in all seven patients, accompanied by a decrease in salivary secretion in six patients and dystrophic articular changes in half of them. All the glands, however, functioned during menstruation. The sensory nerves seemed normal, although there was a disturbance in the secretory centers in the absence of menstruation. The author believes that there are in the circulating blood some substances that affect first the salivary and lacrimal centers and then the glands themselves; during menstruation these substances are neutralized. Then, again, there may be substances that activate the salivary-lacrimal centers, but these substances appear only during menstruation. None of the patients had enlarged lymph nodes or thymus persistens. The patients all had the symptoms of ovarian hypofunction. Believing that ovarian dysfunction was the underlying etiologic factor, the author incorporated in his treatment injections of ovarian extract with surprising improvement and recovery in all but one patient (in whom salivary secretion was increased but the general semeiology was unchanged). The author does not believe that ovarian hypofunction is the primary factor in the cause of the symptom complex. The endocrine glands are all interrelated and there may also be a disturbance in other glands.

Thyroid in Relation to Serum-Atropine Reaction and Serolipoid Content.—Osnovina-Lomovitskaya asserts that her experiments do not prove that the serum-atropine reaction can be used as a test for thyroid function nor can it be related to the serum-lipoid content. There is also no parallelism between serum-lipoid content and the thyroid function. In some patients with clinical manifestations of thyroid hyperfunction there is an oscillation in the serum-lipoid content. After thyroidectomy the serum-lipoids decrease.

Treatment of Amenorrhea by Means of Physical Therapy and an Extract of Urine from Gravida.—Jelokhovtsev asserts that menstrual disturbances may be physiologic only during pregnancy and lactation. Fifty patients with amenorrhea were included in an experimental study. These included patients from 19 to 33 years old; one group was characterized by congenital dystrophies, menstruation once every five or six months, once a year or not at all (three instances), with general habitus similar to eunuchs; a second group was characterized by decrease in menses subsequent to delivery, prolonged breast feeding or abortion, and hyperinvolution of the uterus and a retrograde depression in ovarian activity; and a third group consisted of patients who had overworked and whose living conditions were bad. Most examinations demonstrated a retrograde growth in the size of the uterus, atrophic uterus and cystic ovaries; associated with these there were various chronic inflammatory processes of the adnexa and the pelvic region. In treatment, the author used a sex hormone of the anterior lobe of the hypophysis extracted from the urine of a gravida. He found that the extract, when injected alone, gave good results in 33⅓ per cent of the cases; physical therapeutic agents such as ultraviolet rays, diathermy, baths, ionization with calcium iodide, quartz lamp and local electrotherapy produced improvement in 20 per cent of the patients; but a combination of physical therapy and the hormone produced improvement in 60 per cent. The hypophyseal extract did not seem to be dangerous to the patient, and intravenous injection of from 30 to 40 cc. of it did not cause intoxication in the dog.

Hospitalstidende, Copenhagen

74: 1047-1090 (Nov. 5) 1931

*Clinical Aspect and Etiology of Sarcoid of Boeck. A. Kissmeyer.—p. 1047.
Congenital Dyslexia in School Children. H. Rønne.—p. 1080.
*Demonstration of Tubercle Bacilli in Stomach Lavage Water and Significance of Examination in Diagnosis of Pulmonary Tuberculosis in Adults and Children. V. Clausen.—p. 1084.

Clinical Aspect of Sarcoid of Boeck.—Kissmeyer studied about 200 cases of sarcoid of Boeck from the literature and personally investigated thirty-five cases. He finds that clinically and pathologically it is a definite, universal, benign, extremely chronic and torpid condition, the pathologic-anatomic basis for which is a chronic, inflammation-like granulation tissue characterized by well defined foci, often built up almost homogeneously of epithelioid cells, occurring in the skin, mucous membranes, lymph nodes, bone marrow and other organs, without tendency to necrotic degeneration, but inclined to spontaneous involution. Etiologically it remains a problem for the future to solve.

Demonstration of Tubercle Bacilli in Stomach Lavage Water.—Clausen's examination of the stomach lavage water in 136 adults and 152 children revealed tubercle bacilli in about 50 per cent of the adults with "abacillary" pulmonary tuberculosis and in about 55 per cent of the children with pulmonary tuberculosis.

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